HISTOMORPHOLOGICAL SPECTRUM OF MALIGNANT UTERINE NEOPLASMS

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I hereby declare that the thesis entitled "**HISTOMORHOLOGICAL SPECTRUM OF MALIGNANT UTERINE NEOPLASMS**" submitted towards partial fulfillment of the requirements for the award of **MD in Pathology** degree to BFUHS is a compilation of original work carried out by me under the supervision of Dr Aminder singh, Associate Professor, Dr. Neena Sood, Former Professor & Head, and Dr. Harpreet Kaur, Professor & Head, Department of Pathology. No part of this thesis has formed the basis for the award of any degree previously.

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Dedicated
to
my
Family
&
Teachers

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Learning is not attained by chance; it requires blessings of a teacher to learn and grow

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Dr. Sargun Grewal

LIST OF ABBREVIATIONS

FIGO	International Federation of Gynecology and Obstetrics
EC	Endometrioid carcinoma
SC	Serous carcinoma
CCC	Clear cell carcinoma
ULMS	Uterine leiomyosarcoma
LGESS	Low grade endometrial stromal sarcoma
HGESS	High grade endometrial stromal sarcoma
MMMT	Malignant mixed Mullerian tumor
NKSqCC	Non-keratinizing squamous cell carcinoma
KSqCC	Keratinizing squamous cell carcinoma
ECC	Endocervical adenocarcinoma
SCNEC	Small cell neuroendocrine carcinoma
ER	Estrogen receptor
PR	Progesterone receptor
MMR	Mismatch repair
PTEN	Phosphatase and Tensin
CK	Cytokeratin
WT1	Wilms' tumor 1
EMA	Epithelial membrane antigen
SMA	Smooth muscle actin
WHO	World health organization
IHC	Immunohistochemistry

ABSTRACT

Introduction- Histopathological analysis is mandatory for diagnostic and therapeutic purposes in all uterine neoplasms.

Objectives- To study the histomorphological spectrum of malignant uterine neoplasms and correlate with IHC findings wherever possible.

Materials and methods-The present study was a prospective and retrospective study on histomorphological spectrum of malignant uterine neoplasms of specimens received in the Department of Pathology, Dayanand Medical College & Hospital, Ludhiana over a period of 5 years (3.5 years retrospectively from 1st July 2016 to 31st December 2019 and 1.5 years prospectively from 1st January 2020 to 30th June 2021). During this period all the specimens were analysed with respect to light microscopy and correlated with IHC findings wherever available.

Results- Total of 239 malignant uterine neoplasms were received during the study period, out of which 202 were of uterine corpus and 37 of uterine cervix with a mean age of 58.2 years and post-menopausal bleeding being the commonest clinical presentation seen in 60.25% cases. One sixty-six (82.18%) cases of malignant uterine corpus neoplasms were epithelial in origin with endometrioid carcinoma being the commonest histological subtype accounting for 150 (90.36%) cases followed 13 (7.83%) cases of serous carcinoma. FIGO grade I endometrioid carcinoma predominated comprising 66% of the cases. Maximum cases were of leiomyosarcoma accounting for 9 (50%) cases amongst malignant mesenchymal neoplasm of uterine corpus. All the 18 cases of malignant mixed epithelial and mesenchymal neoplasms were of carcinosarcoma with presence of heterologous sarcomatous components in 7 (38.88%) cases. Non-keratinizing squamous cell carcinoma was the commonest malignant neoplasm of cervix accounting for 64.86% cases. Overall, the immunohistochemical panel commonly comprised of ER, PR, WT1, p53, p16, PAX8, vimentin, CK7, CK20 and Ki-67. Other markers such as Napsin A, CD10, Cyclin D1, desmin, SMA, myogenin, CK5/6, p40 were used depending on the histological impression.

Conclusion –Uterine neoplasms are a heterogeneous group of tumors and are diagnostically challenging. Correlation of histomorphological diagnosis with immunohistochemistry (wherever possible) is important to give a definitive diagnosis as the management varies for different histological subtypes.

Keywords- malignant, uterus, cervix, epithelial, mesenchymal, immunohistochemistery (IHC)

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INTRODUCTION

Endometrial carcinoma is the most common invasive neoplasm of the female reproductive tract. Worldwide, approximately 319,600 cases are diagnosed each year, making endometrial carcinoma the sixth most common cancer in women.[1] Factors associated with unopposed estrogenic stimulation, such as obesity and exogenous hormone use, as well as the presence of endometrial hyperplasia, are commonly related to the development of most of the endometrial carcinomas.The majority of patients have a favorable outcome, but some women die from their neoplasm within a few years of treatment; these high-risk patients can be identified on the basis of pathologic characteristics.

Endometrial carcinoma is not a single disease, but a heterogeneous mix of cases consisting of tumors of different grades and histotypes.Histological grade is one of the most important prognosticators and is used to determine the need for adjuvant treatment. It is classified morphologically on the basis of a combination of growth patterns and cytological features into endometrioid, serous, clear cell and mucinous carcinoma. De-differentiated tumors occur in a small subset of cases.These are graded on the basis of the percentage of solid growth pattern and nuclear features into low-grade and high-grade tumors. Endometrioid and mucinous carcinomas are considered typically low-grade whereas serous, clear cell, and de-differentiated carcinomas are all considered high grade.[2]

Uterine sarcomas comprise a group of rare tumors with differing tumor biology, natural history and response to treatment. Diagnosis is often made following surgery for presumed benign disease. Currently, preoperative imaging does not reliably distinguish between a benign and malignant pathology. Uterine leiomyosarcoma is the most common sarcoma, but other subtypes include endometrial stromal sarcoma (low grade and high grade), undifferentiated uterine sarcoma and adenosarcoma.Amongst these, leiomyosarcomas are the commonest in

India as proved by a retrospective study conducted over a period of 8 years by Nusrath et al, in which total of 11 cases of uterine sarcoma were diagnosed. Out of these, 6 patients had leiomyosarcoma (54.5%), 4 had endometrial stromal sarcoma (36%), and 1 had adenosarcoma (9%).The incidence of uterine sarcoma is 3%–7% of all uterine malignancies and is associated with a poor prognosis when compared to endometrial carcinoma.[3]

Despite the widespread screening programs, cervical cancer remains the fourth most common cancer among women globally and the second most common cancer among Indian women. India alone bears 23% of the global cervical cancer burden.[4]

Tumors arising in the ectocervix are most often squamous cell carcinomas and tumors arising from the endocervix are more likely to be adenocarcinomas.Squamous carcinoma is the most common type of cervical carcinoma, accounting for 75% of invasive cervical carcinoma cases, followed by adenocarcinoma.Nevertheless,over the last three decades, a significant increase in adenocarcinoma cases has been observed in many developed countries, especially in younger women. Adenosquamous, small cell or neuroendocrine, serous papillary, and clear cell carcinomas of the cervix are less common histological subtypes.[5]

Persistent infection with human papillomavirus (HPV) is considered the major cause of cervical cancer. Although the sensitivity of HPV testing has improved significantly in recent years, a small fraction of cases are reported as HPV-negative and are associated with poor prognosis.

The common pathological types of HPV-positive adenocarcinoma are intestinal, villoglandular, signet-ring cell, and endometrioid adenocarcinoma. These originate from the cervical squamo-columnar junction zone, accounting for nearly 90% of all cervical adenocarcinomas. The pathological types of HPV-negative cervical adenocarcinoma are gastric, clear cell, serous, and mesonephric adenocarcinomas. These are quite rare and there occurrence might be non HPV- related.It is estimated

that approximately 5.5–11% of cervical cancers worldwide are HPV-negative. A review of 243 studies and 30,848 women with invasive cervical cancer that were reported between 1990 and 2010 revealed a gradual decrease in the number of HPV-negative cases.[6]

AIMS AND OBJECTIVES

To study the histomorphological spectrum of malignant uterine neoplasms and correlate them with IHC wherever possible.

REVIEW OF LITERATURE

Development and Anatomy of Uterus

Paramesonephric ducts formed by invagination of coelomic epithelium, fuse in the midline to form the uterovaginal canal (or uterine canal). It gives origin to the uterine tubes, the uterus, and part of the vagina. The epithelium of uterus develops from the fused part of paramesonephric ducts. The myometrium is derived from surrounding mesoderm.As the thickness of the myometrium increases, the unfused horizontal parts get partially embedded within its substance, and help to form the fundus of the uterus.The uterine tubes also develop from the unfused parts of the paramesonephric ducts.

The adult nulliparous uterus is a hollow, pear- shaped organ measuring about 7-8 cm along its longest axis and weighing 40-80g. It is broadly divided into the corpus uteri and cervix uteri. The corpus further subdivides into fundus, body and isthmus. Fundus corresponds to the line connecting the insertion of the fallopian tubes. Isthmus connects the corpus to the cervix and the the part between fundus and isthmus forms the body of corpus uteri.[7]

Histology of Uterus

The uterine cavity is triangular shaped and is lined by inner mucosal endometrium which is surrounded by the thick muscular myometrium and an outer serosal covering. Endometrium is divided into three histologically and functionally distinct layers. Deepest or the basal layer is stratum basalis, adjacent to the myometrium and undergoes little change during menstrual cycle. The intermediate layer is broad and composed of spongy appearing stroma and is called stratum spongiosum. The superficial layer is thinner and has compact stromal appearance and is known as the stratum compactum. The glands of the endometrium are lined by tall columnar cells some of which bear cilia and the stroma is composed of stromal cells having plump spindle shaped nuclei with scant cytoplasm.

The myometrium is composed of interlacing bundles of slender long fibres arranged in longitudinal, transverse and oblique sections.

Cervix forms the lower portion of the uterus connecting it to the vagina through the endocervical canal. The outer surface forms the ectocervix and the portion related to endocervical canal forms the endocervix. Most of the ectocervix is covered by a nonkeratinizing squamous epithelium and the glandular mucosa of the endocervix is formed by a layer of mucus secreting tall columnar cells. The area where this squamous and glandular epithelium meet is the squamocolumnar junction.[8]

Vascular and Lymphatic Supply of Uterus

The blood supply to the uterus is via the uterine artery and the venous drainage is via a plexus in the broad ligament that drains into the uterine veins.

Branches of the uterine arteries pass through the myometrium and divide into straight arteries and spiral arteries. Straight arteries are short and pass a small distance in the endometrium and bifurcate to form a plexus that supplies the stratum basalis. Spiral arteries are long and coiled and pass to the surface of the endometrium giving of many branches which form a capillary plexus around glands and stratum compactum.

The uterine lymphactics drain to a rich network of lymph nodes, the main groups being parametrial and paracervical; internal, external and common iliac; periaortic and inguinal.[9]

WHO (2014) classification for malignant tumors of uterine corpus [10]

Malignant Epithelial tumours:

1) Endometrioid carcinoma

   i) Squamous differentiation
   ii) Villoglandular
   iii) Secretory

2) Serous carcinoma

3) Clear cell carcinoma

4) Mucinous carcinoma

5) Mixed cell adenocarcinoma

6) Undifferentiated carcinoma

7) Dedifferentiated carcinoma

8) Neuroendocrine tumors

a) Low grade neuroendocrine tumors
   i) Carcinoid tumor
b) High grade neuroendocrine carcinoma
   i) Small cell neuroendocrine carcinoma
   ii) Large cell neuroendocrine carcinoma

Malignant Mesenchymal tumours:

1) Leiomyosarcoma
   - Epithelioid leiomyosarcoma
   - Myxoid leiomyosarcoma sarcoma

2) Endometrial stromal sarcoma
   - Low-grade endometrial stromal sarcoma
   - High-grade endometrial stromal sarcoma
3) Undifferentiated uterine sarcoma
4) Miscellaneous
   - Rhabdomyosarcoma
   - Malignant Perivascular epithelioid cell tumour

Malignant mixed epithelial and mesenchymal tumors

- Adenosarcoma
- Carcinosarcoma

Lymphoid and myeloid tumors

Secondary tumors

WHO (2020) classification for malignant tumors of uterine corpus [11]

Malignant Epithelial tumours:

1. Endometrioid adenocarcinoma NOS
2. Serous carcinoma NOS
3. Clear cell adenocarcinoma NOS
4. Mucinous carcinoma, intestinal type
5. Mixed cell adenocarcinoma
6. Undifferentiated carcinoma NOS
7. Mesonehphric adenocarcinoma
8. Squamous cell carcinoma NOS
9. Mesonephric-like adenocarcinoma
10. Carcinosarcoma NOS

Malignant Mesenchymal tumours:

1) Leiomyosarcoma NOS
   - Epithelioid leiomyosarcoma
   - Myxoid leiomyosarcoma
   - Spindle leiomyosarcoma

2) Endometrial stromal sarcoma
   - Low-grade endometrial stromal sarcoma
   - High-grade endometrial stromal sarcoma

3) Undifferentiated uterine sarcoma

4) Rhabdomyosarcoma

5) Malignant Perivascular epithelioid cell tumour

Malignant mixed epithelial and mesenchymal tumors

- Adenosarcoma

Miscellaneous tumors

1. Primitive neuroectodermal tumor NOS
2. Germ cell tumors NOS
- Yolk sac tumor NOS
- Immature teratoma NOS

Comparison of the 2014 And 2020 Classification

The new WHO classification 2020 has abolished the term malignant mixed mullerian tumor for carcinosarcoma and now classifies it under endometrial epithelial neoplasms. It is now accepted that the sarcoma is derived from the carcinoma as a result of trans-differentiation (epithelial-

mesenchymal transition) during tumor evolution. The category of mucinous carcinoma, defined by mucinous cells involving > 50% of the tumor, has been eliminated**.**Novel subtypes of endometrial carcinoma including mesonephric-like carcinoma and gastric (gastrointestinal)-type mucinous carcinoma have been added.Mesonephric-like carcinoma is characterized by a variety of architectural patterns, focal intraluminal eosinophilic secretions and nuclei resembling papillary thyroid carcinoma with mild to moderate atypia. They are often GATA-3, TTF-1, calretinin, and CD10 (luminal) positive, with ER negative or at most focally positive. Gastrointestinal-type mucinous carcinoma is composed of mucin-secreting glands (+/- goblet cells) with low-grade atypia and may be mismatch repair protein-deficient.Amongst the malignant mesenchymal neoplasm, spindle cell variant of leiomyosarcoma has been added to the classification. Specific diagnostic criteria for myxoid leiomyosarcoma are proposed: presence of any cytological atypia, tumor cell necrosis or > 1 mitoses/10 HPF.

Considering the study period of the present study, the neoplasms were categorised and the observations were compiled as per the 2014 WHO classification.

MALIGNANT EPITHELIAL TUMORS OF UTERINE CORPUS

Endometrioid Carcinoma-Endometrioid carcinoma is the most common form of endometrial carcinomas, accounting for more than three-fourths of all cases. These tumors are referred to as endometrioid because they resemble proliferative-phase endometrium**.** They account for approximately 80% of endometrial adenocarcinomas.

Precursor lesions-Endometrial hyperplasia represents a spectrum of morphological endometrial alterations. It is predominantly characterized by an increase in the endometrial gland-to-stroma ratio when compared to normal proliferative endometrium. It is categorised as:

Hyperplasia without atypia- It is an exaggerated proliferation of glands of irregular size and shape, with an associated increase in the gland to

stroma ratio compared with proliferative endometrium, but without significant cytological atypia. Some glands may have normal coiled architecture, others branch or are cystically dilated. These are lined by stratified columnar type epithelium, with frequent mitotic figures.

Atypical hyperplasia/ endometrioid intraepithelial neoplasia- It is composed of crowding of cytologically atypical tubular or branching glands with little intervening stroma. The features of nuclear atypia include enlargement, pleomorphism, nuclear rounding, and loss of polarity and presence of nucleoli. It is often associated with squamous but also secretary and mucinous metaplasia.

It is seen that amongst females with endometrial hyperplasia and without treatment, approximately 25% of women with atypical hyperplasia developed carcinoma as compared to only 3% women with hyperplasia without atypia. Both these lesions are associated with exposure to unopposed estrogen leading to abnormal proliferations. However, it is clear that the presence of nuclear atypia represents a fundamental change that predisposes women to development of carcinoma.[12]

Grossly they can be focal, diffuse or composed of separate polypoid masses. The typical appearance is pale tan to white and soft, but can occasionally firm. Foci of haemorrhage, necrosisis often visible, especially in poorly differentiated tumors. Myometrial invasion by similar tissue is grossly evident in some cases. Myometrial invasion usually appears as well-demarcated and firm, grey-white tissue with linear extensions beneath an exophytic mass. However, it may also present as multiple, white nodules with yellow areas of necrosis within the uterine wall. Extension into the lower uterine segment or the isthmus is common. The involvement of cervix occurs in approximately 20% of cases.

On microscopy typical endometrioid carcinomas are composed of tubular glands, most of which are medium sized, round to oval but may be angulated or branched. They often form anastomosing cribriform masses with fusion of the neoplastic glands. These glands are lined by stratified or

pseudostratified columnar cells with rounded nuclei and variably prominent nucleoli with moderate amount of pale to lightly eosinophilic cytoplasm. Nuclear pleomorphism is most often only mild to moderate. The histologic grade of endometrial adenocarcinoma is related to the aggressiveness of the tumor and probability of death from disease. In 1988, the International Federation of Gynaecology and Obstetrics (FIGO) revised its recommendations for grading typical endometrial adenocarcinoma. The grade is determined primarily by the architecture of the tumor and secondarily modified in the presence of notable nuclear atypia.

Based on glandular and solid architecture: Grade 1 tumors exhibit ≤5% solid nonglandular, nonsquamous growth;Grade 2 tumors from 6% to 50%; Grade 3 tumors>50%. The solid tumor growth is best considered non-squamous when nuclear features in the solid areas are similar to those seen in the glandular component of the tumor.

The presence of marked cytologic atypia increases the grade 1 level. Since mucinous adenocarcinomas of the endometrium are closely related to endometrioid carcinomas, it is reasonable to use FIGO grade for those carcinomas as well. All of the other endometrial tumor types carry an intrinsic tumor grade (i.e., serous, clear cell, and de-differentiated carcinomas and carcinosarcomas are high grade)

The nuclear grade of a tumor was assigned based upon the features displayed by the majority of the neoplastic cells.Nuclear grade was defined as – Grade 1: uniform round to oval nuclei, even distribution of chromatin and inconspicuous nucleoli; Grade 2: irregular oval nuclei, chromatinclumping and moderate size nucleoli; Grade 3: large, pleomorphic nuclei, coarse chromatin, and large irregular nucleoli.

The implication of this classification was that the patients with architectural grade 1 tumors, but with either grade 2 or grade 3 nuclei, were now being designated as FIGO grade 2. Similarly patients with architectural grade 2 tumors but with grade 3 nuclei will be designated as FIGO grade 3. It is

observed that upgrading on the basis of grade 3 nuclear criteria was appropriate and useful as approximately 20% more patients were assigned to grade 3, a group for whom adjuvant therapy is generally recommended.

Endometrial carcinoma can display myometrial invasion in different forms.It can either invade along a broad pushing manner or can infiltrate the myometrium diffusely as masses or clusters of cells and individual glands. Such carcinomas with diffusely infiltrative pattern of invasion share the same prognostic indicators of clinically aggressive disease as those having the more conventional pattern of myometrial invasion.

Morphological Variants of Endometrioid Carcinoma:

- **Endometrioid carcinoma with squamous differentiation-** These tumors account for approximately 25% of endometrioid carcinomas. The squamous element should constitute at least 10% of a tumor to qualify as an adenocarcinoma with squamous differentiation. They contain rounded nests, often called morules,of squamous cells typically occupying the lumens of the neoplastic glands. They are composed of immature polygonal to occasionally spindled squamous cells with bland nuclear features. Sometimes, the cells may undergo maturation and even keratinization. In adenosquamous carcinomas,the squamous epithelium may be intraglandular but is often independently invasive of the endometrium or myometrium in contrast to the morules of endometrioid carcinoma with squamous differentiation.
- **Endometrioid carcinoma with secretory differentiation-** Endometrioid carcinomas in which glycogen vacuoles (subnuclear, supranuclear, or both) are present within most of the neoplastic cells are said to have secretory differentiation. Consequently, they resemble endometrial glands of the secretory phase. An unusual pattern, it represents only 1–2% of endometrial carcinomas.Classic

endometrioid carcinomas with secretory differentiation are almost always well differentiated.

- **Villoglandular endometrioid carcinoma-** Villoglandular endometrioid carcinomas are characterized by long, slender, finger like papillae with thin fibro vascular cores. The cells lining the villi and glands resemble those of typical endometrioid carcinoma. Mitotic activity is variable and myometrial invasion usually is superficial.[13]

TNM Classification of Carcinomas Of Uterine Endometrium (WHO 2014)

T – Primary tumour

TX Primarytumour cannot be assessed

T0 No evidence of primary tumour

Tis Carcinoma in situ (preinvasive carcinoma)

T1 Tumour confined to the corpus uteri

T1a Tumour limited to endometrium or invading less than half of myometrium

T1b Tumour invades one half or more of myometrium

T2 Tumour invades cervical stroma, but does not ex- tend beyond the uterus

T3 Local and/or regional spread as specified below

T3a Tumour invades the serosa of the corpus uteri or adnexae (direct extension or metastasis)

T3b Vaginal or parametrial involvement (direct extension or metastasis)

T4 Tumour invades bladder/bowel

N – Regional Lymph Nodes

NX Regional lymph nodes cannot be assessed

N0 No regional lymph node metastasis

N1 Metastasis to pelvic or para-aortic lymph nodes

N2 Metastasis to para-aortic lymph nodes with/without metastasis to pelvic lymph nodes

M – Distant Metastasis

M0 No distant metastasis

M1 Distant metastasis (excluding metastasis to vagina, pelvic serosa, or adnexae, including metastasis to inguinal lymph nodes other than para-aortic or pelvic nodes)

Molecular pathogenesis of endometrioid carcinoma has led to a better understanding of its immunophenotype. The preponderance of FIGO grade 1 and 2 endometrioid carcinomas express estrogen receptor (ER) and progesterone receptor (PR) and approximately one-half of FIGO grade 3 endometrioid carcinomas without serous, clear cell, or undifferentiated features are also ER/PR positive.

P53 overexpression resulting from TP53 mutation and accumulation of mutant p53 protein is rare in FIGO grade 1 adenocarcinomas and only in a minority of FIGO grade 2 adenocarcinomas.But present in a significant number of FIGO grade 3 adenocarcinomas. However, when p53 staining is prominent, serous, clear cell or undifferentiated tumors should be considered**.**

Another common molecular alteration in endometrioid carcinoma is the molecular phenotype of MSI. Lynch syndrome, also known as hereditary nonpolyposis colorectal cancer (HNPCC) syndrome, an autosomal-dominant inherited cancer susceptibility syndrome caused by a germline mutation in one of the DNA mismatch repair genes, accounts for the majority of inherited cases of endometrial carcinoma. Mutations in one of the four mismatch repair genes*,* MLH1, MSH2, MSH6 or PMS2 have been identified in patients with Lynch syndrome.[14]

Role of p16 has been analysed in endometrioid carcinoma in order to distinguish it from serous carcinomas and endocervical adenocarcinomas. Majority of grade 3 endometrioid carcinomas are more likely to be focally positive for p16 and show wild-type staining for p53. Serous carcinomas and endocervical carcinomas on the other hand usually show a diffuse strong positivity for p16. However, exceptions to this typical staining

pattern occur in both tumor types and in general a panel of markers is the most reliable approach.[15]

Serous carcinoma-Serous carcinoma is characterized by a complex papillary and/or glandular architecture with diffuse, marked nuclear pleomorphism. What distinguishes serous carcinoma from these other types is the uniformly marked cytologic atypia.

Grossly it is often inconspicuous, arising on the surface of an endometrial polyp. Since these tumours mostly arise in elderly women, the uterus is usually small, but it may be enlarged by tumour distending the uterine cavity.

On microscopy a complex papillary architecture is characteristic of the pure form of uterine serous carcinoma although a solid growth pattern and glandular architecture may occur. The papillae may be short, branching and hyalinized or long, thin and delicate. These have fibro vascular cores. Each papilla is lined by epithelial cells with large atypical nuclei, prominent nucleoli and scant to moderate cytoplasm with a clear or eosinophilic appearance. The luminal surface often appears scalloped. Psammoma bodies are found in one-third of cases. Pleomorphic/bizarre forms are often present. Numerous mitotic figures are usually found.

A serous carcinoma with a prominent glandular pattern lacking papillary features may be confused with an endometrioid carcinoma. In this case, it is predominantly the nuclear morphology that aids in the distinction. The glands in an endometrioid carcinoma have a smooth luminal border and are lined by columnar cells with nuclei that are grade 1 or 2. Endometrioid carcinomas with grade 3 nuclei are almost always solid, not glandular. In contrast, the glands in a serious carcinoma are lined by cells with high-grade nuclei, some of which are hobnail shaped, thus are imparting a scalloped luminal border to the glands. In addition, in most cases papillary tufts project or lie detached in the gland lumens. Immunohistochemical analysis can aid in the distinction of glandular serous carcinoma from endometrioid carcinoma.

On immunohistochemistry a basic panel includes at least p53 and p16 along with either ER or PTEN**.**It is found that the majority of serous carcinomas is negative for ER and PR, positive for PTEN, diffusely positive for p16 and exhibit aberrant mutation-type expression (diffusely and strongly positive or entirely negative) with p53. On the other hand, grade 3 endometrioid carcinomas are more likely to be positive for ER and PR, negative for PTEN, focally positive for p16 and show wild-type staining for p53.(22). WT1 is usually negative in endometrioid carcinomas.However, it has been found to be focally positive (in up to 30% of cases) in uterine serous carcinoma.[16]

Clear Cell Carcinoma-It is composed of polygonal or hobnail-shaped cells with clear or eosinophilic cytoplasm arranged in a papillary, tubulocystic or solid pattern, with at least focal high-grade nuclear atypia.The prevalence of clear cell carcinoma ranges from 1% to 6%**.** These tumors do not have distinctive gross features.

Clear cell carcinoma on microscopy display at least one of 3 architectural patterns: solid, papillary, and/or tubulocystic. The tubulocystic pattern is the most commonly encountered, and is at least focally present in most cases but the papillary pattern is most frequently (28%–41%) predominant.

Papillary pattern- The papillae of clear cell carcinoma are most commonly in the form of small rounded papillae.Other papillary patterns include architecturally complex papillae with hierarchical branching, micropapillae, long and slender papillae.These are lined by hobnail, cuboidal, or polygonal cells with clear or eosinophilic cytoplasm. There is no significant nuclear stratification, cellular tufting, or detached cellular budding.

Tubulocystic pattern -Represents a morphologic spectrum from glands/tubules to cystic formations. The glands are relatively uniform and display rounded contours with open lumina. Increasing cystic dilatation of the glands is usually accompanied by less confluence, although fully cystic

units may also be entirely confluent. Tubular glands are linedby hobnail cells. Cystic glands may be lined by similar cells or by a bland, flat cellular population. The interglandular stroma may be hyalinized, myxoid or fibroblastic. Extensive nuclear stratification, cellular tufting, or detached cellular budding is not seen.

Solid pattern-It is almost invariably admixed with other patterns and is characterized by diffuse sheets of polygonal cells with well-defined cell borders, with interspersed thin fibrous septa. Clear cells usually predominate in the solid areas, although a conspicuous population of oxyphilic cells is not infrequent.

Typical immunohistochemical profile of clear cell carcinoma is HNF1B-positive, Napsin A-positive, ER and PR-negative and p53-wild-type.Approximately 40% of clear cell carcinomas harbor TP53 mutations and show diffuse p53 immunohistochemical expression.They are usually negative for CK20 and WT1, and lack diffuse, strong cytoplasm expression of CEA. Clear cell carcinomas are typically ER/PR negative and show p16 and Ki-67 expression that are intermediate between endometrioid and serous carcinomas.[17]

Mucinous Carcinoma-An endometrial carcinoma, in which > 50% of the neoplasm is composed of mucinous cells**.** Itis a rare histologic type representing less than 5% of all endometrial carcinomas.On gross examinationmucinous carcinomas can be suspected by their gelatinous or mucoid texture.

Mucinous carcinomas are almost always well differentiated and have a relatively good prognosis. They tend to display a glandular or villoglandular architecture lined by uniform, mucinous, columnar cells with minimal stratification. Nuclear atypia is mild and mitotic activity is low. Myometrial invasion is typically limited to the inner-half.

The distinction of mucinous carcinoma of the endometrium from clear cell or secretory carcinoma is made on the basis of morphology and PAS and mucin stains like mucicarcmine. The mucin is recognized as basophilic

globules or slightly pale, granular cytoplasm which is positive for mucicarmine and CEA.

Other than CEA a panel of immunohistochemical markers including MUC1, p16, ER, PR, and valentine is recommended. MUC1 has been found to be positive in majority of endometrial mucinous adenocarcinoma (EMMA) cases when compared to endocervical adenocarcinomas. ER and PR have been found to be positive in 90% of the cases Staining for p16 is positive in about only 20% cases and Vimentin in nearly 50%.[18]

Mixed Cell Adenocarcinomas-Mixed endometrial carcinoma is composed of two or more different histological types of endometrial carcinoma, with at least one being grade II category.

By convention, a mixed carcinoma has at least one other component comprising at least 10% of the tumor. The most commonly encountered mixture is endometrioid with serous carcinoma.Immunohistochemistry may clarify the presence of two distinct cell types.

A combination of PTEN, p53, and p16 helps to discriminate between endometrioid and serous carcinoma. Almost all serous carcinomas display aberrant p53 staining and diffuse staining for p16.On the other hand endometrioid carcinomas display a patchy distribution of p16. Also, PTEN expression is lost in endometrioid carcinoma but generally not in serous carcinoma [19]

Undifferentiated and Dedifferentiated Carcinoma-The 2019 WHO defined undifferentiated endometrial carcinoma as a tumor lacking any evidence of differentiation. Dedifferentiated carcinoma, on the other hand is one in which undifferentiated carcinoma is associated with FIGO grade 1 or 2 endometrioid carcinoma.Most undifferentiated carcinomas form large, polypoid, intraluminal masses ranging from 2–15 cm in size. Necrosis is common. Most tumours involve the uterine corpus; however, many involve the lower uterine segment.

On morphology it is a monomorphic neoplasm composed of small to intermediate-sized cells arranged in sheets without any obvious glandular

differentiation. They frequently exhibit a characteristic “dyscohesive” pattern and raises a differential diagnosis of lymphoma, plasmacytoma, high-grade endometrial stromal sarcoma or small cell carcinoma

Additional morphologic features that are present in some undifferentiated and dedifferentiated carcinomas include focal alveolar, nested and vaguely corded or trabecular growth patterns, rhabdoid/plasmacytoid morphology (vesicular nucleus containing a large nucleolus and abundant pink cytoplasm) focal marked nuclear pleomorphism, multinucleation, spindling, and “abrupt” keratinization

When present, the differentiated low-grade endometrioid component is typically found lining the endometrial cavity, with the undifferentiated component present deep to it. This may account for a diagnosis of low-grade endometrioid carcinoma in a biopsy specimen and dedifferentiated carcinoma at hysterectomy.

Undifferentiated carcinomas and dedifferentiated carcinomas together represent ~10% of high-grade endometrial carcinomas and hence about 2% of endometrial carcinomas overall.[20]

The majority of undifferentiated carcinomas (and the undifferentiated component of dedifferentiated carcinoma) lack expression of PAX8, ER, and PR but up to 20% of tumors may show focal staining with these markers .More than 80% of undifferentiated carcinomas display evidence of epithelial differentiation in the form of intense EMA and cytokeratin (especially cytokeratin 18) staining of a small proportion of tumor cells.Loss of expression of MLH1 and PMS2, mostly due to MLH1 promoter methylation is seen in ~50% to 60% of cases. Rare cases with germline DNA MMR gene mutations diagnostic of Lynch syndrome have been reported.[21]

Neuroendocrine Carcinoma-A diverse group of neoplasms that share a morphological neuroendocrine phenotype. Neuroendocrine tumours are rare, representing < 1% of endometrial cancers. It includes both small cell and large cell variants. Approximately 90 cases of endometrial small cell

NECa (SCNECa) have been reported in the literature to date.Studies of endometrial large cell NECa (LCNECa) are even less common, with only 15 cases reported in the literature.

Usually produces a bulky, exophytic, polypoid intraluminal mass with variable myometrial invasiongrossly.In SCNEC the growth pattern may be diffuse, trabecular, nested or have rosette-like structures is composed of poorly cohesive ovoid cells, having condensed chromatin and scant cytoplasm. Nuclear moulding, mitotic figures, necrosis and apoptotic bodies are frequent. LCNECs are arranged in well demarcated nests, trabeculae or cords with peripheral palisading. Tumour cells are large, polygonal, with vesicular or hyperchromatic nuclei and a prominent nucleolus. There is mitotic activity is high and extensive geographic necrosis is often noted.

On immunohistochemistry theycommonly react for chromogranin A, synaptophysin, CD56, vimentin and dot-like pattern ofcytokeratins.[22]

MALIGNANT MESENCHYMAL TUMORSOF THE UTERINE CORPUS

Uterine Leiomyosarcoma(ULMS)-A malignant smooth-muscle tumour, most commonly displaying spindle cell morphology but occasionally showing epithelioid or myxoid features. It represents about 1.3% of uterine malignancies and >50% of uterine sarcomas, excluding carcinosarcoma.

These present as solitary intramural masses grossly having a soft or fleshy appearance with poorly defined margins. Most ULMS irregularly invade the adjacent myometrium and have a cut surface that is usually pale with areas of hemorrhage and necrosis. An important feature is the loss of the sharp line of demarcation that separates tumor from the normal myometrium.

ULMS is composed of fascicles of spindle cells with abundant eosinophilic cytoplasm. The nuclei are fusiform, with rounded ends and are hyperchromatic having coarse chromatin and prominent nucleoli.Cellular pleomorphism can be marked in poorly differentiated neoplasms.

Multinucleated tumor cells are found in 50% of ULMS's. Vascular invasion is noted in 10-22% of ULMS's.

The main criteria used to diagnose leiomyosarcoma of the uterus are the presence of moderate to severe degree of nuclear atypia, a high mitotic index (≥10 MF/10 HPF) and a coagulative tumor cell necrosis which is seen as an abrupt transition between the necrotic and viable cells. In contrast, a hyaline type necrosis shows a distinct zonal pattern having a centre of bland necrosis and a periphery of granulation tissue with bands of hyalinized collagen in between. Tumors with coagulative necrosis but neither atypia nor increased mitotic activity should be diagnosed as Smooth muscle tumor of uncertain malignant potential (STUMP)[23]

Morphological Variants of ULMS:

Epithelioid Leiomyosarcoma-These are composed of round to polygonal cells and exhibit one of the cell of epithelioid differentiation. The leiomyoblastoma pattern is the most common, although clear cell epithelioid leiomyosarcoma have also been reported. The usual features of malignancy seen in conventional ULMS are generally present which are cytological atypia, tumor cell necrosis and high mitotic rate.

Myxoid Leiomyosarcoma-These are large gelatinous neoplasms that usually appear to be well circumscribed. The smooth muscle cells are separated by myxoid material. The characteristic low cellularity is partly due to presence of only few mitotic figures per high power fields in most myxoid ULMS. Other features include myometrial infiltration and vascular invasion.

TNM Classifictaionof Uterine Sarcomas (WHO 2014)

T – Primary tumour

T1 Tumour limited to the uterus

T1a Tumour 5cm or less in greatest dimension

T1b Tumour more than 5cm in greatest dimension

T2 Tumour extends beyond the uterus, within the pelvis

T2a Tumour involves adnexa

T2b Tumour involves other pelvic tissues

T3 Tumour involves abdominal tissues

T3a One site in abdomen

T3b More than one site in abdomen

T4 Tumour invades bladder or rectum

N – Regional Lymph Nodes

NX Regional lymph nodes cannot be assessed

N0 No regional lymph node metastasis

N1 Regional lymph node metastasis

M – Distant Metastasis

M0 No distant metastasis

M1 Distant metastasis (excluding adnexa, pelvic and abdominal tissues)

IHC is usually not required for the diagnosis of ULMS, but is occasionally necessary to differentiate ULMS from other uterine malignancies such as undifferentiated endometrial sarcoma or sarcomatoid carcinoma. It is reported thatKi-67 overexpression, with an accompanying loss of ER and PR expression in case of LMScorrelated with worsened long-term prognosis for the patient. Bcl-2, a protein encoded in humans by the BCL2 gene, plays a major role in the regulation of apoptosis.High Bcl-2 exression predicted longer disease-specific survival in women with uterine LMS. A combination of clinic pathologic parameters including Ki-67 and Bcl-2 protein expression allows us to distinguish groups of LMS with different survival, and that tumors that were Ki-67 positive and Bcl-2 negative had worse prognosis.

Mutations in the TP53 gene which encodes the p53 protein are correlated with unfavorable prognosis for the affected patients. The expression of p16, p53 and Ki-67 is stronger in uterine LMS as compared to normal leiomyomas (LMs), LM variants, and STUMP.[24]

Endometrial Stromal Sarcoma-ESS was originally divided into low-grade and high-grade based on mitotic count. The 2003 WHO classification system eliminated the ‘high-grade’ category and reclassified these

tumours into ‘ESS’ (low-grade tumours with histological resemblance to proliferative endometrial stroma) and ‘undifferentiated endometrial sarcoma’ (pleomorphic tumours with no resemblance to endometrial stroma). Subsequently, it has become increasingly evident that the ‘undifferentiated endometrial sarcoma’ category is too broad, encompassing a wide range of heterogeneous tumours with different clinical behaviour and outcome, and that at least a subset of these tumours are morphologically and genetically distinct. Thus both 2014 and the 2020 WHO classification scheme now incorporates recent molecular findings into the classification, dividing these into endometrial stromal nodule (ESN), low-grade endometrial stromal sarcoma (LGESS), high-grade endometrial stromal sarcoma (HGESS) and undifferentiated uterine sarcoma (UUS).

Low Grade Endometrial Stromal Sarcoma (LGESS)-They may be submucosal or intramural, usually with ill-defined borders and ‘wormlike’ permeation within the myometrium and parametrial tissue, the cut surface is fleshy tan to yellow.Areas of haemorrhage, necrosis and cystic degeneration might be present.

Tumourcells grow in sheets and are typically small with scant cytoplasm wth a uniform, oval to fusiform nuclei. They show minimal to no cytological aypia and low-mitotic activity (usually < 5 per 10 HPF) although higher counts may occur. A delicate network of arterioles is common. The ‘tongue-like’ patterns of myometrial and lymphovascular invasion are classical histological features that are important in the distinction. Variant histological features include smooth muscle differentiation (‘star-burst’ appearance), rhabdomyoblastic, rhabdoid, fibromyxoid, sex-cord, glandular, collagen plaques and others.

On Immunohistochemistry LGESS is positive for CD10, ER andPR. However, CD10 is not entirely specific and may stain some smooth muscle tumours, especially leiomyosarcoma and almost 50% of highly cellular leiomyomas. Therefore, it is important to use a panel that includes

CD10 and at least two smooth muscle markers (eg, desmin, h-caldesmon, smooth muscle heavy chain myosin) as there is no single marker that is specific for ESS.

High Grade Endometrial Stromal Sarcoma (HGESS)-The tumours may be seen as intracavitary polypoidal or intramural masses with or without obvious myometrial invasion. Size typically ranges up to 9cm and can often show extra-uterine extension at the time of diagnosis. Cut surface shows a tan to yellow, fleshy appearance with occasionally areas of haemorrhage and necrosis.

On low power it infiltrates the myometrium in a manner similar to that of low-grade endometrial stromal sarcoma. The microscopic appearance is variable, ranging from low-grade spindle cell areas to a high-grade uniform small round cell component. The round cell areas are hyper cellular and the cells are arranged in vague to well defined nests and separated by a delicate capillary network. The round cells have a modest amount of eosinophilic to granular cytoplasm, irregular nuclear contours and granular to often vesicular chromatin, with variably distinct nucleoli. Necrosis is usually present. The spindle cell component usually has fibromyxoid features. Lymphovascular invasion is typically present. It lacks conspicuous pleomorphism and mitotic activity is typically greater than 10 MF/10 HPF, in contrast to low-grade endometrial stromal sarcoma.Rarely, a high-grade sarcoma is seen in association with areas that have the appearance of conventional low-grade endometrial stromal sarcoma and also can be diagnosed as high-grade endometrial stromal sarcoma.

On immunohistochemistrythe high-grade component of tumour is CD10, ER and PR negative but shows strong diffuse cyclin D1 positivity (> 70% nuclei), whereas the low-grade spindle cell component is typically strongly anddiffusely CD10, ER and PR positive and shows variable, heterogeneous cyclin D1 expression.

p53 staining shows a wild-type pattern of positivity while pankeratin, EMA, SMA, desmin, caldesmon, S100, HMB45, and Melan-A are negative.The

expression of hormone receptors was associated with favorable survival outcome in ESS.[25]

Undifferentiated Uterine Sarcoma- A tumour arising in the endometrium or myometrium, lacking any resemblance to proliferative-phase endometrial stroma, with high-grade cytological features and with no specific type of differentiation. They are often intraluminal polypoid masses, usually > 10 cm, with a fleshy cut surface and areas of necrosis and/or haemorrhage.

Undifferentiated uterine sarcoma is an aggressive uterine sarcoma subtype that lacks morphologic and immunophenotypic evidence of cell differentiation. Previously known as “undifferentiated endometrial sarcomas,” these tumors may arise in the endometrium or myometrium and consist of highly atypical cells arranged in sheets and storiform or herringbone patterns. Destructive myometrial invasion, brisk mitotic activity, tumor necrosis, and vascular involvement are frequently present.

These tumours are variably CD10 positive and ER and PR weakly positive or negative. Cyclin D1 can be diffusely positive but in those cases the tumours are also typically positive for CD10. Focal smooth muscle actin, desmin, EMA or keratin positivity may be seen.

Pleomorphic and uniform undifferentiated uterine sarcomas also appear distinct with estrogen (ER) and progesterone receptors (PR) as well as beta-catenin and cyclin D1 more frequently expressed among uniform tumors and aberrant p53 staining patterns limited to pleomorphic ones.

MALIGNANT MIXED EPITHELIAL AND MESENCHYMAL TUMORS OF UTERINE CORPUS

Adenosarcoma-Uterine adenosarcomas are rare. They are a biphasic tumor composed of both a sarcomatous stroma and a benign epithelium. The sarcomatous component is usually low-grade and homologous to uterine sarcoma. The epithelium consists of endometrium-like cells commonly.

Recent data based on National Cancer study of 2,205 cases showed that the primary sites were the uterine corpus (n = 1,884), the uterine cervix (n = 229), and the ovary (n = 92). This corresponded to 0.43% for uterine, 0.16% for cervical, and just 0.04% for ovarian malignancies.[26]

The uterine cavity is typically filled with a polypoidal and lobulatedmass which might be projecting through the cervical so. Cut surface may show cystic areas with focal hemorrhage and necrosis.

The epithelial element is seen as glands separated by the abundant stromal component.Mostly the epithelium is endometrioid in type, though it can also be ciliated, mucinous, and occasionally squamous type.The stromal component is often low grade, composed of spindled and/or round cells. One of the most characteristic features of adenosarcoma is the formation of “periglandular cuffing” seen as stromal cells concentrating about the glandular elements, forming a cuff or so-called ‘‘cambium’’ layer. A stromal mitotic activity 2 or more per 10 HPFs is required for a diagnosis of adenosarcoma.

Adenosarcomas have heterologous stromal elements which may vary from scattered rhabdomyoblasts with crossstriations to sex cordlike elements, composed of nests, cords, solid, or hollow tubules. The sex cord-like elements may contain abundant eosinophilic or foamy cytoplasm. Two cases have recently been reported with extensive overgrowth of sex cord-like elements within an adenosarcoma.[27]

TNM classification for Adenosarcoma of the uterine corpus (WHO 2014)

T – Primary tumour

T1 Tumour limited to the uterus

T1a Tumour limited to the endometrium/endocervix

T1b Tumour invades less than half the myometrium

T1c Tumour invades one half or more of the myometrium

T2 Tumour extends beyond the uterus, within the pelvis

T2a Tumour involves adnexa

T2b Tumour involves other pelvic tissues

T3 Tumour involves abdominal tissues

T3a One site

T3b More than one site

T4 Tumour invades bladder or rectal mucosa

N – Regional Lymph Nodes

NX Regional lymph nodes cannot be assessed

N0 No regional lymph node metastasis

N1 Regional lymph node metastasis

M – Distant Metastasis

M0 No distant metastasis

M1 Distant metastasis (excluding adnexa, pelvic and abdominal tissues

In most adenosarcomas with a low-grade stromal component without sarcomatous overgrowth, the stromal element expresses ER, PR, CD10, and WT1. It is negative for p53 and exhibits a low MIB1 proliferation index. Typical adenosarcomas showed a strong stromal reactivity for CD10.The immunostaining is weaker in adenosarcomas with sarcomatous overgrowth.It was observed that the loss of PR immunoexpression in stromal component of adenosarcomas with sarcomatous overgrowth and carcinosarcomas was more compared with typical adenosarcomas [28]

Carcinosarcoma- A biphasic tumour composed of highgrade carcinomatous and sarcomatous elements. The tumour is characteristically large and polypoid, filling the entire uterine cavity and often protruding through the cervical os. On cut section it is typically soft, with areas of haemorrhage, necrosis and cystic degeneration. There is frequent myometrial invasion and sometimes cervical involvement.

There is an admixture of high-grade epithelium and mesenchymal component; either of the two may predominate. The two components are usually distinct and sharply demarcated. The epithelium is most often of endometrioid or serous types. The mesenchymal component is a high-grade, non-specific sarcoma. Often heterologous elements including

rhabdomyosarcoma, chondrosarcoma and osteosarcoma are seen in 50% of cases. Neuroectodermal differentiation may rarely occur. These tumours commonly exhibit deep myometrial and lymphovascular invasion.The immunophenotype parallels that of the individual elements. Panel of markers includeER,PR,androgen receptor (AR), CD10, WT1, smooth muscle actin, desmin, AE1/3 cytokeratin, CD34, calretinin, inhibin, c-kit, and Ki-67.

The final diagnosis of carcinosarcoma is based on histologic evidence of a dual population of carcinomatous and sarcomatous cells with invasion of the stroma, the complete diagnosis is typically based on pathologic evaluation following hysterectomy.

Other Rare Malignant Tumors

Rhabdomyosarcoma is heterologous malignant mesenchymal tumor with skeletal muscle differentiation. They are grossly very bulky. Microscopically, it can present as pleomorphic, embryonal, alveolar or spindle- cell rhabdomyosarcoma. Pleomorphic rhabdomyosarcoma shows admixture of markedly atypical spindled and polygonal cells. Embryonal rhabdomyosarcoma is characterized by small round to oval cells with hyperchromatic nuclei and scanty cytoplasm. Subepithelial condensation of the tumorcells (cambium layer) is noted.Alveolar rhabdomyosarcoma shows cells arranged in loose alveoli containing non-cohesive round cells with moderate eosinophilic cytoplasm whereas the spindle-cell rhabdomyosarcoma shows fascicles of spindled cells with brightly eosinophilic cytoplasm and cross-striations.

Malignant perivascular epithelioid tumor is mesenchymal tumor presenting as a pelvic mass with AUB in perimenopausal women. It is composed of epithelioid cells having eosinophilic, granular cytoplasm showing melanocytic and smooth muscle differentiation, thought to have derived from the perivascular epithelioid cells. Parameters that impact the prognosis are size (>5cm), infiltrative margins, high grade nuclear atypia, cellularity, mitosis (>1/50HPF), necrosis and vascular invasion. Tumor

cells exhibit positivity for Melan-A, HMB45, SMA. Desmin and h-caldesmon expression is less common.

Germ cell tumors like teratomas and yolk sac tumors can develop in the endometrium either in pure forms or in association with endometrioid carcinoma.

Malignant lymphomas can present initially in the endometrium and myometrium or both. Most common are diffuse large B cell lymphomas. Cases of marginal zone lymphoma, T- cell lymphoma, granulocytic sarcoma, plasmacytoma and hodgkins lymphoma have also been reported.

Metatstatic carcinomas form breast, gastrointestinal tract, kidney and skin (melanomas) are the most frequent primary sites.[8]

WHO (2014) classification for malignant tumors of uterine cervix[10]

Malignant Squamous epithelial tumors

Squamous cell carcinoma, NOS

- Keratinizing
- Non-keratinizing
- Papillary
- Basaloid
- Warty
- Verrucous
- Squamotransitional
- Lymphoepithelioma-like

Malignant Glandular tumours

- Adenocarcinoma, NOS
  - Endocervicaladenocarcinoma, usual type
  - Mucinous carcinoma, NOS
- Adenoid basal carcinoma
- Adenoid cystic carcinoma
- Undifferentiated carcinoma
- Neuroendocrine tumors
  a) Low grade neuroendocrine tumors
     i) Carcinoid tumor
     ii) Atypical carcinoid tumor
  b) High grade neuroendocrine carcinoma

Malignant mixed epithelial and mesenchymal tumors

- Adenosarcoma
- Carcinosarcoma

Malignant mesenchymal tumors

- Leiomyosarcoma
- Rhabdomyosarcoma

i) Gastric type
ii) Intestinal type
iii) Signet-ring cell type

- Villoglandular carcinoma
- Endometrioid carcinoma
- Clear cell carcinoma
- Serous carcinoma
- Mesonephric carcinoma
- Adenocarcinoma admixed with neuroendocrine carcinoma

➢ Adenosquamous carcinoma
- Glassy cell carcinoma

- Alveolar soft-part sarcoma
- Angiosarcoma
- Malignant peripheral nerve sheath tumour
- Liposarcoma
- Undifferentiatedendocervical sarcoma
- Ewing sarcoma

Germ cell tumours

- Yolk sac tumor

Lymphoid and myeloid tumours

Secondary tumors

WHO (2020) classification for malignant tumors of uterine cervix[11]

Malignant Squamous epithelial tumors

1) Squamouscell carcinoma,HPV-associated
2) Squamous cell carcinoma,HPV-independent
3) Squamous cell carcinoma, NOS

Malignant Glandular tumours

1) Adenocarcinoma, NOS
2) Adenocarcinoma, HPV- associated
3) Adenocarcinoma, HPV- independent, gastric type
4) Adenocarcinoma, HPV- independent, intestinal type
5) Adenocarcinoma, HPV- independent, mesonephric type

Malignant mixed epithelial and mesenchymal tumors

- Adenosarcoma

Germ cell tumours

- Yolk sac tumor
- Endodermal sinus tumor
- Choriocarcinoma

6) Adenocarcinoma,HPV-independent,NOS
7) Endometrioid adenocarcinoma NOS
8) Carcinosarcoma NOS
9) Adenosquamous carcinoma
10) Mucoepidermoid carcinoma
11) Adenoid basal carcinoma
12) Carcinoma, undifferentiated, NOS

Comparison Of the 2014 And 2020 classification

Carcinomas in both squamous and glandular categories are now classified as HPV-associated and HPV-independent. There are currently no morphologic clues to distinguish between HPV-associated and HPV-independent squamous cell carcinomas.Adenocarcinoma in-situ also now has two recognized categories: HPV-associated (frequently referred to as “usual”) and HPV-independent. Currently, only gastric-type AIS and atypical lobular endocervical glandular hyperplasia belong to the latter category. They feature foamy clear to eosinophilic mucinous cytoplasm, distinct cell borders, nuclear atypia and intraglandular growth (tufting, micropapillary, cribriform). HPV-independent adenocarcinomas, in particular gastric-type adenocarcinoma, have worse clinical behavior than HPV-associated adenocarcinomas.HPV-associated endocervical adenocarcinomas represent 85-90% of all adenocarcinomas. Their histologic hallmark is the presence of conspicuous apical mitoses and apoptosis.They are characterized by p16 overexpression (strong and diffuse, nuclear and cytoplasmic staining), normal p53 staining and negative to weak ER/PR staining.The usual subtype is the most common, defined as having < 50% of cells with intracytoplasmic mucin, with the remaining having non-mucinous cytoplasm.The mucinous subtype, defined as having > 50% cells with intracytoplasmic mucin, can feature endocervical-type mucinous epithelium or intestinal-type

epithelium.Gastric-type adenocarcinoma represents the most common type of HPV-independent adenocarcinoma (~10% of all adenocarcinomas). It features epithelium with foamy clear to eosinophilic mucinous cytoplasm and prominent cell borders.p53 can show mutant-type expression, and p16 can be strong and diffuse.

Other recognized types of HPV-independent adenocarcinoma are clear cell and mesonephric. Endometrioid and serous carcinomas of the cervix are exceedingly rare, and their diagnosis requires first exclusion of an endometrial and tubo-ovarian primary.

TNM Classification OfTumors of Uterine Cervix (WHO 2014)

TX Primary tumour cannot be assessed

T0 No evidence of primary tumour

Tis Carcinoma in situ (preinvasive carcinoma)

T1 Tumour confined to the cervix (extension to corpus should be disregarded)

T1a Invasive carcinoma diagnosed only by microscopy. Stromal invasion with a maximal depth of 5.0 mm measured from the base of the epithelium and a horizontal spread of 7.0 mm or less

T1a1 Measured stromal invasion 3.0 mm or less in depth and 7.0 mm or less in horizontal spread T1a2 Measured stromal invasion more than 3.0 mm and not more than 5.0 mm with a horizontal spread of 7.0 mm or less

Note:The depth of invasion should be taken from the base of the epithelium, either surface or glandular, from which it originates. The depth of invasion is defi need as the measurement of the tumour from the epithelial–stromal junction of the adjacent most superficial papillae to the deepest point of invasion. Vascular space involvement, venous or lymphatic, does not affect classification.

T1b Clinically visible lesion confined to the cervix or microscopic lesion >T1a

T1b1Clinically visible lesion 4.0 cm or less in greatest dimension

T1b2 Clinically visible lesion more than 4.0 cm in greatest dimension

T2 Tumour invades beyond uterus but not to pelvic wall or to lower third of vagina

T2a Tumour without parametrial invasion

T2a1 Clinically visible lesion 4.0 cm or less in greatest dimension

T2a2 Clinically visible lesion more than 4.0 cm in greatest dimension

T2b Tumour with parametrial invasion

T3 Tumour extends to pelvic wall, involves lower one- third of vagina,causes hydronephrosis or non- functioning kidney

T3a Tumour involves lower one-third of vagina

T3b Tumour extends to pelvic wall, causes hydrone- phrosis or nonfunctioningkidney

T4 Tumour invades mucosa of the bladder or rectum, or extends beyond true pelvis

Notes: All macroscopically visible lesions even with superficial invasion are T1b/IB. Vascular space involvement, venous or lymphatic, does not affect classification. Bullous oedema is not sufficient to classify a tumour as T4. Invasion of bladder or rectal mucosa should be biopsy proven according to FIGO.

N – Regional Lymph Nodes

NX Regional lymph nodes cannot be assessed

N0 No regional lymph node metastasis

N1 Regional lymph node metastasis

M – Distant Metastasis

M0 No distant metastasis

M1 Distant metastasis (includes inguinal lymph nodes and intraperitoneal disease except metastasis to pelvic serosa). It excludes metastasis to vagina, pelvic serosa, and adnexa.

Squamous Cell Carcinoma (SCC) Cervix

An invasive epithelial tumour composed of squamous cells of varying degrees of differentiation.Certain genotypes of human papillomavirus

(HPV) have been shown to be critically associated with the development of uterine cervical cancer.About 6.6% of women in the general population are estimated to harbor cervical HPV infection. HPV serotypes 16 and 18 account for nearly 76.7% of cervical cancer in India, HPV 16 being the predominant genotype related to SCC of the uterine cervix.[30]

On gross examination they may be predominantly exophytic, papillary or polypoid. Endophytic tumours covered by normal epithelium, or tumours arising in the portion of the cervical canal that are not visible or accessible to sampling, may be clinically occult.

Most carcinomas exhibit sheet-like growth and infiltrate as bands or single cells with an intervening desmoplastic or inflammatory stroma.Three cellular variants of cervical squamous cell carcinoma exist, although admixtures and intermediate forms abound: large cell non-keratinizing, keratinizing and small cell.

Non-keratinizing tumours are composed of polygonal squamous cells growing in sheets or nests, but keratin pearls are not present. Cellular pleomorphism is more obvious and mitotic figures are usually numerous. The nuclei are relatively large with coarsely granular chromatin and nucleoli may be irregular or multiple.

Keratinizing tumours contain keratin pearls, abundant keratohyaline granules. They display dense cytoplasmic keratinization. The nuclei are usually large and hyper chromatic with coarse chromatin.

Small cell tumours are composed of smaller cells with a very high nuclear to cytoplasmic ratio and less prominent nucleoli. They may overlap on histology with ‘small cell carcinomas’ of the cervix. The latter term should be reserved for tumours that are neuroendocrine in nature.

Basaloid squamous cell carcinoma is an aggressive variant of SCC wherever in the body it has been described and hence the tumour is considered high-grade they are composed of nests of immature, basal-type squamous cells with scanty cytoplasm. Some individual cell keratinization may be present but keratin pearls are rarely seen. The

nuclei may be quite pleomorphic, and high mitotic counts and “comedo-like” necrosis are frequent.

Verrucous carcinoma is a highly differentiated squamous cell carcinoma thatinvades the underlying stroma in the form of bulbous epithelial pegs with a pushing border. Because these tumours may have very thick epithelium, superficial biopsy or cytology may underestimate the severity of the disease process. The tumour cells have abundant cytoplasm, and their nuclei show minimal atypia and do not exhibit infiltrative growth.

Warty/condylomatous squamous cell carcinoma is defined as a squamous cell carcinoma with a warty surface and low-power architecture analogous to a condyloma. In early invasive lesions the epithelium may be keratinizing. Cells displaying changes analogous to koilocytic atypia.

Papillary squamous cell carcinoma is a tumour in which thin or broad papillae with connective tissue stroma are covered by epithelium showing the features of high grade squamous intraepithelial lesion (HSIL). A superficial biopsy may not reveal evidence of invasion but complete excision of the clinically visible lesion reveals an underlying invasive tumour of the usual type.

Squamotransitional carcinoma is rare transitional cell carcinomas of the cervix that are indistinguishable from their counterparts in the urinary bladder. They may occur in a pure form or may contain malignant squamous elements. These tumors demonstrate papillary architecture with fibro vascular cores, lined by a multilayered, atypical epithelium resembling HSIL.

Lymphoepithelioma-like carcinoma is a rare tumour in the cervix. Histologically, it is strikingly similar to the nasopharyngeal tumour of the same name. It is composed of poorly defined islands of undifferentiated squamous cells in a background intensely infiltrated by lymphocytes. The tumour cells have uniform, vesicular nuclei with prominent nucleoli and moderate amounts of slightly eosinophilic cytoplasm. The cell borders are indistinct, often imparting a syncytial-like appearance to the groups. The

tumours of the cervix are most likely HPV-related as are all cervical cancers.

On immunohistochemistry**,** p63, p40, and cytokeratin 5/6(CK5/6) are the most common panel of immunochemical markers for the diagnosis of squamous carcinoma. p63 and CK5/6 are traditional markers that indicate squamous differentiation.p40 is a new specific marker for distinguishing squamous carcinomas from adenocarcinoma, whose specificity is about 100%.

MUC5AC could be expressed in other adenocarcinomas and might be used for the differential diagnosis of adenocarcinoma and squamous carcinomain the setting of absent or diminished p63 and cytokeratin 5/6 staining.Diffuse p16 positivity in the cervix in most cases is associated with high risk HPV infection and can be regarded as a surrogate marker of the presence of high risk HPV.The combined detection of Ki-67 and p16 protein has a high application prospect as an auxiliary diagnosis of SCC. [31]

Cervical Adenocarcinoma

Cervical adenocarcinomas span a diverse group of tumors with several distinct histologic tumor types, which include endocervical, endometrioid, intestinal, villoglandular, gastric, signet ring, serous, clear cell, and mesonephric.Cervical adenocarcinomas have traditionally been subclassified based on tumor cell type, but this is slowly giving way to a classification i.e., HPV associated versus HPV independent. The basis for this shift is the recognition that the morphologic features and prognosis are significantly different for tumors in these two major categories.

Human Papilloma Virus–Associated Cervical Adenocarcinoma

The HPV-associated tumors account for a large majority of cervical adenocarcinomas. These tumors present no distinguishing gross characteristics compared to their squamous cell counterparts.

Composed of glands with cyto-architectural atypia that infiltrates the cervical stroma. A surface component with a papillary architecture may

also be prominent. In some adenocarcinomas, particularly those that are high-grade, non-specific patterns such as nests, clusters and individual cells are seen. Criteria for early invasion include frankly infiltrating glands or tumour cells nests, extension of atypical glands beyond the depth of the normal endocervical glands, neoplastic endocervical glands that are too complex to be adenocarcinoma in situ or with stromal reaction in the form of oedema, chronic inflammation or desmoplasia.

Morphologic Variants:

Endocervical adenocarcinomas they show high mitotic rate, numerous apoptotic bodies, and strong diffuse p16 positivity, as well asfrequent admixture with more conventional appearing HPV-associated cervical adenocarcinoma.

Serous (papillary) carcinoma is analogous in appearance to the homonymous uterine and ovarian neoplasm, including the common occurrence of psammoma bodies. Primary cervical serous ADC is exceedingly rare; most serous adenocarcinomas involving the cervix are malignancies spreading directly from the endometrium or metastases from a primary ovarian, tubal, or peritoneal serous adenocarcinoma.

Villoglandular (papillary) adenocarcinoma presents as an exophytic polypoid lesion with papillae lined by endocervical, endometrial, or intestinal-type epithelium showing only mild atypia. At the base they show smooth contoured glands, without infiltrative features, and these may be in situ lesions. This diagnosis should not be made based on a small biopsy as there may be conventional invasive cervical adenocarcinoma underlying and a diagnosis of “well-differentiated villoglandular adenocarcinoma” will suggest a very favorable prognosis that does not reflect the underlying infiltrative component.

Adenosquamous (mixed) carcinoma combines adenocarcinoma with a well-defined squamous component. Adenosquamous carcinoma should be distinguished from squamous cell carcinoma without glandular formations but with histochemically demonstrable intracellular mucin.

Glassy cell carcinoma has been described as a distinct type of poorly differentiated adenosquamous carcinoma. It occurs in a younger age group (mean age, 41 years) than other cervical neoplasms and often has been associated with pregnancy. The tumor cells have a moderate amount of cytoplasm with a groundglass or finely granular appearance, a prominent eosinophilic and PAS-positive cell membrane, and large nuclei with prominent nucleoli. Mitoses are numerous. A prominent inflammatory infiltrate, often rich in eosinophils, is regularly seen in the adjacent stroma, and this may be accompanied by peripheral blood eosinophilia. The prognosis is poor.

Adenoid cystic carcinoma is a specific variant of cervical adenocarcinoma that tends to occur in elderly multigravid women of and is associated with a particularly poor prognosis.The morphologic appearance is similar to that of the homonymous tumors of salivary glands. Like the former, it may be cribriform (the most common pattern) or grow in a predominantly solid fashion. Adenoid cystic differentiation may be present admixed with other patterns of HPV-associated cervical adenocarcinoma.

Adenoid basal carcinoma (tumor; epithelioma) should be distinguished both from adenoid cystic carcinoma and from basaloid (squamous cell) carcinoma. Although it shares many phenotypic features with adenoid cystic carcinoma, it is a very low-grade lesion, in contrast with the two neoplasms with which it can be confused.The consistent presence of oncogenic HPV has been documented.

Other variants of endocervical adenocarcinoma, all of them exceedingly rare, are a microcystic type, a signet ring type, a small intestinal (enteric) type, and a type with choriocarcinomatous and hepatoid differentiation.

HPV-Independent Cervical Adenocarcinomas

Although the sensitivity of HPV testing has improved significantly in recent years, a small fraction of cervical cancers are continued to be reported as HPV-negative. HPV-negative cervical cancer is often diagnosed at an advanced FIGO stage and associated with poor prognosis.It is estimated

that approximately 5.5–11% of cervical cancers worldwide are HPV-negative.

Morphologic Variants:

Gastric-type adenocarcinoma- Characterized by well-formed glands lined by cells with voluminous clear or eosinophilic cytoplasm and distinct cell borders. Gastric ADCs may show a spectrum of differentiation from very well-differentiated areas lacking atypia and categorized as minimal-deviation adenocarcinoma to areas with moderate to marked cytologic atypia, including nuclear enlargement, variations of nuclear shapes, and the presence of macronucleoli. They lack the high mitotic rate.

Gastric ADC is negative for ER and PR and demonstrates cytoplasmic positivity for CEAthe staining for p16 is typically negative, correlating with negative HPV status; however, a small percentage of cases may show strong, blocklike p16 positivity.Approximately 41% of the cases show mutation-type p53 staining with either diffuse strong positivity (24%) or null pattern (17%).[32]

Clear cell carcinoma -The histologic features of clear cell ADC are similar to those of the more common clear cell adenocarcinomas of the endometrium or ovary. Similarly, 3 architectural patterns are observed: tubulocystic, papillary, and solid. The fibrovascular cores in the papillary pattern may show characteristic hyalinization. Glands are lined by large cells with abundant clear cytoplasm are characteristic.“Hobnail” cells are common, as are intraglandular papillary projections. Grossly, the tumor is usually exophytic. This tumor type is rare now, but there was a cluster of cases in young women associated with diethylstilbestrol (DES) exposure in utero. Cervical clear cell carcinomas are positive for hepatocyte nuclear factor-1b, 8 as well as napsin-A, similar to their ovarian and uterine counterparts. Despite negative HPV status, the tumors may show positivity for p16 with a spectrum from focal to diffuse. They are negative for CEA, ER, and PR, and most show wild-type p53 expression.

Mesonephric (adeno)carcinoma is a very rare tumorthat develops from the mesonephric duct remnants located deep in the lateral cervical stroma.Numerous architectural patterns of growth were described, including tubular, ductal, papillary, retiform, sex cord–like, solid, and sarcomatoid, and these patterns may be seen in various proportions within the same tumor. The characteristic feature of tumors forming glandular spaces is the presence of deeply eosinophilic intraluminal secretions similar to those present in benign mesonephric proliferations The immunohistochemical profile is similar to that of mesonephric rests and includes positivity for CD10, GATA3, and calretinin.It is diffusely and strongly positive for PAX8, negative for ER, and shows only patchy cytoplasmic staining for p16.[33]

Endometrioid Cervical Adenocarcinoma

An adenocarcinoma arising in the cervix that has endometrioid morphological features. These tumours are morphologically similar to endometrioid adenocarcinomas arising in the uterine corpus. Hence the most important differential diagnosis is with endometrial adenocarcinomas of endometrioid type extending from the uterine corpus.

The morphologic overlap of endometrial and endocervical adenocarcinoma is difficult on H&E. This distinction is important, since the choice of initial therapy may differ substantially as well as differences in chemotherapeutic agents used to treat advanced cases of these tumors. A combination of estrogen receptor (ER), progesterone receptor (PR), vimentin, and CD10 negativity along with carcinoembryonic antigen (CEA), diffuse p16, CD34, and HPV positivity suggests cervical adenocarcinoma, while a combination of ER, PR, vimentin, diffuse p16, and CD10 positivity along with CEA, CD34, and HPV negativity suggests uterine adenocarcinoma.[34]

Neuroendocrine carcinoma

The 2014 WHO classification divides this category into Low-grade neuroendocrine tumor (carcinoid or atypical carcinoid) and High-grade

neuroendocrine carcinoma (small cell or large cell type). Low-grade neuroendocrine tumor of the cervix is vanishingly rare. Small cell and large cell neuroendocrine carcinoma have a similar age distribution as squamous cell carcinoma and has also been found in association with HPV. Large cell neuroendocrine carcinomas show variable arrangement of tumor cells seen as organoid, trabecular, insular, glandular and spindle pattern of growth, while small cell neuroendocrine cracinomas are composed of monomorphic hyperchromatic round to oval cells with scant amount of cytoplasm. On immunohistochemistry positivity for CD56, chromogranin and synaptophysin may be found. p16 expression suggests association with HPV in tumor genesis and can be further confirmed on molecular level.[10]

Other Rare Malignant Neoplasms

Leiomyosarcoma accounts for <1% of malignant cervical tumors and present as masses that expand the cervix grossly. The diagnostic criteria are same as those in the uterine corpus. Smooth muscle markers such as SMA, desmin, h-caldesmon are positive on immunohistochemistry.

Rhabdomyosarcomas are a group of malignant tumors showing skeletal muscle differentiation. They typically present as fleshy polyps with areas of haemorrhage. On microscopy they are composed of small round to spindled hyperchromatic nuclei. Skeletal muscle differentiation can be seen. The tumor cells show positivity for desmin (cytoplasmin) and myogenin (nuclear).

Alveolar soft part sarcomas very rarely present as primary tumors of the cervix. They are composed of large polygonal cells with granular eosiniphilc cytoplasm, arranged in a solid or alveolar pattern. No specific immunohistochemical marker is recognized.

Adenosarcoma accounts for approximately 2% of tumors of female genital tract. No relation to HPV has been reported. Like their counterparts in uterine corpus, they are composed of benign or atypical glands and a

malignant high grade sarcomatous overgrowth. The glands here are lined by endocervical- type epithelium.

Carcinosarcoma presents as large fleshy masses generally occurring in postmeopausal women. Association with HPV has been recognised in contrary to their uterine corpus counterparts. The carcinomatous component more commonly resembles cervical epithelial tumors (basaloid squamous cell carcinoma, adenoid cystic carcinoma, adenoid basal carcinoma).

Malignant lymphomas present as a sub epithelial mass without obvious ulceration. Most often they are diffuse large B cell lymphomas. Granulocytic sarcoma, hodgkinslymphoma and inflammatory pseudotumormay also present initially as cervical masses.

Metastatic carcinomas to the cervix most commonly originate from ovary, large bowel, breast and kidney.[8]

A retrospective study was done by Cirisano et al in 1999 on 574 females undergoing hysterectomy with a clinical stage I-II endometrial cancer,including 53 PapillarySerous(PS) and 18 Clear Cell endometrial carcinomas(CC). The aim of this study was to compare clinical and surgicopathologic staging results for papillary serous (PS) and clear cell (CC) endometrial cancers with endometrioid (EM) carcinoma of the endometrium. PS tumors accounted for 8%, CC for 2%, and EM for 90% of cases. Rates for lymph node metastases were more frequent for PS and CC compared with EM grade 3. When PS tumors were confined to the endometrium, paraaortic metastases occurred in 13%. LVSI increased with EM grade and was highest for PS and CC. The majority of PS and CC tumors were confined to the inner one-third of the myometrium, compared with EM tumors, where grade correlated with depth of myometrial invasion. Extrauterine metastases occurred in 55% of PS and 45% of CC tumors confined to the inner one-half, compared with 17% of EM grade 3. The higher frequency of extrauterine metastases in PS and CC tumors compared with EM, despite similar surgical sampling rates,

supports a more virulent behavior. The poor correlation between depth of myometrial invasion and risk for extrauterine metastases helps to explain poorer survival in PS and CC patients.[35]

Castrillon and associates from Brigham and Women's Hospital in 2002 described a study of 30 endometrial adenocarcinomas and 29 endocervical adenocarcinomas. It included cases that showed overlapping morphologic features, as 15/29 of the endocervical adenocarcinomas showed endometrioid differentiation, and 16/30 of the endometrial adenocarcinomas showed mucinous differentiation. Both sets of tumors were cytokeratin 7 positive and cytokeratin 20 negative. CEA was more common in endocervical adenocarcinomas (62%), than in endometrial adenocarcinomas (27%). The authors also noted that CEA appeared to be particularly useful for tumors that had endometrioid morphology, since only 14% of the endometrial endometrioid adenocarcinomas were CEA positive, in contrast to 67% of the endocervical adenocarcinomas with endometrioid morphology. 97% of the endometrial adenocarcinomas were vimentin positive, often showing a characteristic lateral cell border or perinuclear pattern of reactivity. In contrast, only 7% of the endocervical adenocarcinomas were vimentin positive.[36]

Another study by McCluggage and associates in 2002, evaluated 30 endometrioid endometrial adenocarcinomas and 26 endocervical adenocarcinomas of endocervical type. In their study, 93% of endometrial adenocarcinomas were strongly ER positive, whereas focal weak ER positivity was noted in 38% of endocervical adenocarcinomas. Vimentin was diffusely positive in 97% of the endometrial adenocarcinomas, but in only 8% of the endocervical adenocarcinomas. CEA was seen in 65-95% of endocervical adenocarcinomas. In light of these results, a relatively small panel of immunostains including vimentin, monoclonal CEA, and ER is reasonable to address the problem of distinguishing endometrial from endocervical adenocarcinoma.

Hence they concluded that the “classic” endometrial adenocarcinoma will be positive for vimentin and ER, but negative for CEA. In contrast, the “classic” endocervical adenocarcinoma will be CEA positive and negative for vimentin and ER.[37]

Song et al retrospectively reviewed 59 patients in 2006, to evaluate the clinicopathologic findings and prognostic factors of uterine endometrial cancer. They found that the median age at time of diagnosis was 51 years and Endometrioid adenocarcinoma was the most common (96.6%) histologic type. Forty-nine patients (83.0%) were FIGO stage I and 10 patients were stage II (17.0%), and the histological grades of the tumors were 23 (39.0%) grade 1, 17 (28.8%) grade 2, 7 (11.9%) grade 3, and 12 (20.3%) unknown respectively. The age (> or =60) and menopause state were concluded to be significant prognostic factors of stage I and II uterine endometrial cancer affecting survival of the patients (p=0.0077; p=0.0149, respectively)[38]

In 2009, an immunohistochemical analysis was performed by Yemelyanova et al on 201 uterine and endocervical adenocarcinomas in hysterectomy specimens. This included 49 serous carcinomas, 101 endometrial endometrioid carcinomas (44 FIGO grade 1, 40 FIGO grade 2, and 17 FIGO grade 3), and 51 HPV-related endocervical adenocarcinomas. All serous carcinomas demonstrated diffuse/moderate-strong p16 expression while endometrial endometrioid carcinomas exhibited less diffuse and less intense expression. Similar to serous carcinomas, all endocervical adenocarcinomas exhibited diffuse/moderate-strong p16 expression. Thus, p16 can serve as an additional diagnostic marker, used as part of an immunohistochemical panel, including p53 and hormone receptors, for distinction of uterine serous carcinomas from endometrioid carcinomas. Distinction of serous carcinomas from endocervical adenocarcinomas (HPV-related type), both of which share diffuse p16 expression and frequently lack hormone receptor expression, relies on morphology and diffuse/strong p53 [39]

Another immunohistochemical analysis in 2010 by A. Alkushi et al on 180 endometrial carcinomas included 34 grade 3 endometrioid carcinomas (EC) and 15 serous carcinomas (SC). The purpose of this study was to examine differences in immunophenotype and outcome in a series of high-grade endometrial carcinomas, focusing on the comparison of EC-3 versus SC. It was found that IMP3, ER, PR, PTEN, p53, and p16 were detected in 20%, 82%, 68%, 61%, 39%, and 19% of grade 3 endometrioid carcinomas and 63%, 50%, 46%, 100%, 69%, and 90% of serous carcinomas, respectively.Hence, biomarkers commonly used to distinguish between EC and SC carcinomas such as ER, PR, and p53 are highly effective for the distinction. [40]

In a study done by Sait et al in 2014, a total of 36 patients with uterine sarcoma were reviewed. The median age of all patients was 57 years, and the mean age was 57.72 years. Carcinosarcoma was reported in 21 patients (58%), leiomyosarcoma in 7 (19%), undifferentiated endometrial sarcoma in 6 (17%), and rhabdomyosarcoma in 2 (6%). Approximately half of the patients were stages III and IV (28% and 25%), while 15 patients (41%) were stage I. Only 2 patients (6%) were stage II. The surgical treatment was hysterectomy and bilateral salpingoophorectomy 18 patients (50%), while in 4 patients (19%), debulking was also performed. Cervical involvement was found in 8 (38.1%) in carcinosarcoma and 2 (33%) in undifferentiated endometrial sarcoma. Adnexal involvement was present in 3 (50%) and 7 (33.3%) in undifferentiated endometrial sarcoma and carcinosarcoma. The poor outcome and survival of high-grade uterine sarcoma patients was identified.[41]

A retrospective descriptive study was conducted in 2015 Rubina Mukhtar et al to find the prevalence of cervical carcinoma in Pakistan. Frequency of carcinoma cervix and stage of disease at the time of presentation were recorded. A total of 537 cases were reviewed. Presenting symptoms were irregular vaginal bleeding in 78% patients including, vaginal discharge

was in 29% while pelvic pain was in only 3% patients. Squamous cell carcinoma corresponds to 460 (86.5%), adenocarcinoma to 55 (10.8%) cases and other rare tumours 22 (4%). Only 102 (19%) cases were in Stage Ib, while 247 (46%) were in Stages IIa and Stage IIb respectively, 118 (22%) cases were in Stages IIIa and Stage IIIb, while 57 (10.8%) cases were in advanced stage (1V). It was concluded that squamous cell carcinoma accounted for 86.5% of cases with mean age of 51 years with a high morbidity[42]

A retrospective analysis by Srivani Saravanan et al in 2015 done at a tertiary care hospital included 794 cases of cervical lesions. There were 79.7% cases were non-neoplastic and 20.3% were neoplastic. Only 29 (3.6%) cases and 6 (0.7%) cases occurred before 30 years and after 70 years respectively. Most common type of carcinoma was squamous cell carcinoma with almost equal proportion of keratinizing and non-keratinizing squamous cell carcinomas was observed. No cases of adenocarcinoma were reported in the study. The study highlighted on the spectrum of lesions of the cervix which was further divided under various categories which can provide the basis for identifying the etiology.[43]

Another retrospective and prospective study was done on hysterectomies and punch biopsies by S Srikanth et al in 2016, studied a total of 500 cases for a period of 3 years. Out of the 500 cases, 395 cases were non-neoplastic and 105 cases were neoplastic lesions. Large cell non-keratinizing squamous cell carcinoma was the most common malignant lesion contributing for 28 (26.66%) cases. This was followed by squamous cell carcinoma (2.85%) and adenocarcinoma mucinous type (1.90%).[44]

In 2018, a histological comparison was performed byS. A. Barquet-munoz et al. The aim of the study was to describe the prognostic factors associated with uterine sarcomas. The clinical records between 2000 and 2014 of women diagnosed with uterine sarcomas and initially treated surgically were reviewed.A total of 116 clinical records were reviewed. 32 were classified as carcinosarcomas, 36 (49.3%) were leiomyosarcoma, 18

(24.7%) were undifferentiated endometrial sarcoma, 9 (12.3%) were endometrial stromal sarcoma, and 10 (13.7%) were other histologic subtypes, such as heterologous sarcomas, adenosarcomas, or high-grade sarcomas. The mean age at the time of diagnosis for each histologic subtype was: ESS 41.2 years, UES 54.3 years, LMS 46.6 years, and for the other histologic subtypes 48.1 years. Results demonstrate the importance of an early diagnosis, and thus an early identification of disease that benefits from complete cytoreduction regardless of histology. [45]

In 2019 a study by Nicolas et al., out of 214 cases of cervical adenocarcinoma 21 were HPV negative. 91% had advanced FIGO stage and 67% of these had lymphatic metastasis. Whereas only 57% of HPV associated cases were advanced FIGO stage and only 36% of these has lymphatic metastasis.[46]

A retrospective record based study in 2019 by Anila Tresa Alukal et al analysed 32 diagnosed cases of uterine sarcoma over a period of 5 years (Jan 2010- Dec 2015) to assess the epidemiological aspects, clinical features and histopathological features of uterine sarcomas. The most common histological pattern was carcinosarcoma or Mixed malignant Mullerian tumour 44%, followed by leiomyosarcoma 28%, endometrial stromal sarcoma 22% and undifferentiated stromal sarcoma and adenosarcoma 3% each. MMMT was commonly seen in 60 and above age group whereas leiomyosarcoma and endometrial sarcoma were seen in 40-49 yrs. of age. The most common presenting complaint of MMMT was postmenopausal bleeding. (50%) followed by discharge per vagina and abdominal pain, while for leiomyosarcoma and endometrial stromal sarcoma was heavy menstrual bleeding (67 % and 43% respectively) followed by abdominal pain.[47]

A retrospective analysis of histopathological patterns of carcinoma cervix was done by Manjit Kaur Rana et al in 2019 on a total of 120 cervical biopsies out which 106 cases were of carcinoma cervix. The most

common histopathological type detected was squamous cell carcinoma accounting for 80.1%, followed by 13.2% cases of adenocarcinoma. In this study the least common variant, a type of adenosquamous carcinoma was recognized accounting for 0.97% of total cervical carcinomas and presented with metastasis to solid organs. Other least common types identified were neuroendocrine type (1.8%) and undifferentiated type (1.9%). The most common age group in carcinoma cervix was fifth and sixth decade with history of bleeding per vagina being the most common clinical presentation. Only 2.8% cases underwent Pap smear screening, rest of the cases presented with symptoms of carcinoma. Maximum number of cases presented with stage ≥ II in all ages. The current study stressed the fact that a majority of Indian women are diagnosed at later stages of cervical cancer. There are many variants with different clinical presentations and specific light microscopic features which need to be considered clinically.[48]

Over a 4-year period, 552 cases of endometrial malignancies were reported by Subbaraya et al in 2020 with an objective to characterize endometrial stromal sarcomas (ESSs) using immunohistochemical and molecular markers. Of these, 5 were low grade (LG-ESS) and 3 were high grade (HG-ESS). CD10 was 100% sensitive and 75% specific for LG-ESS. ER and PR were 100% specific but less sensitive (80%) for LG-ESS. All 3 cases of HG-ESS showed diffuse strong cyclin D1 (>70% nuclei) positivity and were negative for cluster differentiation. Hence, CD10 had a sensitivity of 100% and specificity of 90%, and ER/PR showed a sensitivity and specificity of 80% and 100%, respectively, in the diagnosis of LG-ESS. Cyclin D1 expression is highly specific for in HG-ESS (100%).[49]

Hashmi et al in 2020 retrospectively analysed a seven year data from 2013 to 2019, assesing all the patients undergoing radical hysterectomies. Records regarding tumor type, grade, depth of myometrial invasion, and ovarian, omental, nodal, and parametrial involvement were assessed. A total of 129 cases of endometrial carcinoma (EC) were included. The

mean age of the patients was 57.6 ± 9.3 years. Majority of the cases were type 1 ECs (82.2%). The most common histological type of EC was endometrioid (82.2%) followed by serous carcinoma (10.1%). Most of the tumors were grade 1 (42.6%). Nodal metastases were present in eight cases (6.2%) and adnexal involvement was present in 12 cases (9.3%). There was a significant association of the type of EC with lymphovascular invasion, nodal metastasis, and adnexal involvement.[50]

MATERIAL AND METHODS

The present study was a prospective and retrospective study on histomorphological spectrum of malignant uterine neoplasms of specimens received in the Department of Pathology, Dayanand Medical College & Hospital, Ludhiana over a period of 5 years [3.5 years retrospectively from 1st July 2016 to 31st December 2019 and 1.5 years prospectively from 1st January 2020 to 30th June 2021]. During this period the specimens were analysed with respect to light microscopy in all cases and correlated with IHC findings wherever possible for malignant uterine neoplasms.

A total of 71,656 specimens were received during the study period, out of which 239 cases of malignant uterine neoplasms were diagnosed with respect to light microscopy and correlated with immunohistochemical findings wherever possible.

METHOD OF COLLECTION OF DATA

Inclusion criteria:

1. All malignant uterine corpus and cervix specimens.
2. Prepared and stained slides for review for uterine corpus and cervical malignancies from an outside center.

Exclusion criteria: All non- malignant neoplasms of uterine corpus and cervix.

Duration of study: Retrospective 3 ½ years and prospective 1 ½ years.

Study Design: This is prospective and retrospective study.

Outcome: All the findings were documented according to the protocol and categorized according to the WHO classification (2014) for malignant uterine neoplasms. The histomorphological findings were correlated with the IHC findings wherever possible.

Statistical Analysis: Data were described in terms of range; mean, median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. All statistical calculations were done using

SPSS (Statistical Package for the Social Science) SPSS 21 version statistical program for Microsoft Windows.

Methodology: Biopsies and resected specimens were received in containers containing 10% formalin. Random representative sections were taken from the specimen and then were processed. Paraffin embedding and subsequent staining by Hematoxylin and Eosin was done. IHC markers such as ER, PR, WT1, p53, p16, PAX8, vimentin, CK7, CK20 and Ki67. Other markers such as Napsin A, CD10, Cyclin D1, desmin, SMA, myogenin, CK5/6, p40 were done depending on the histological impression.

Paraffin Block Tissue Processing

The tissue fixed in 10 % formalin was processed through a series of solutions in the automatic tissue processor as follows:

- Acid formalin for 4 hours
- Formal alcohol for 1 hour80% ethyl alcohol for 1 hour
- 90% ethyl alcohol for 1 hour
- Absolute ethyl alcohol for 1 hour
- Acetone [1 stchange] for 1 hour
- Acetone [2 nd change] for 1 hour
- Xylene [1 stchange] for 1 hour
- Xylene [2 nd change] for 1 hour
- Paraffin [1 st change at 58-69°C] for 1 hour
- Paraffin [2 nd change at 58-69°C] for 1 hour The paraffin embedded tissue blocks were cut at 2-3um thickness by rotary microtome. The sections were then transferred onto albunimized slides. These sections were labelled properly with the help of glass marking pencil.

Procedure of Hematoxylin and Eosin staining:

- Slides were kept on hot plate in order to dewax the sections at temperature upto 60ºC.
- Then the slides were deparaffinised in xylene

- Then hydration was done by passing through descending rates of alcohol to water.
- The slides were then stained in Harris Hematoxylin for 15 minutes. Sections were washed well in running tap water until sections turned blue. These sections were then differentiated in 1 % acid alcohol [1% HCL in 70% alcohol] for 5-10 seconds, washed well in tap water till sections were again blue for 5 minutes or less.
- These were again stained in 1% Eosin for 10 minutes followed by washing in running tap water for 1-5 minutes.
- Sections were dehydrated once again through ascending grades of alcohol, cleaned in Xylene and mounted with DPX [Distyrenedibutylphtalate xylene] avoiding air bubbles.
- Stained slides were then subjected to microscopic examinations under both [10X] and high power [40X]

Procedure for Immunohistochemical staining-Immunohistochemistry was done in 72cases. Suitable blocks were chosen for IHC. The immunohistochemical stains used were ER, PR, WT1, p53, p16, PAX8, vimentin, CK7, CK20, Ki67, CD10, Cyclin D1, desmin, SMA, p40.

Ventana Benchmark GX was used for immunohistohistochemistry.

Methodology:

Immunohistochemistry

1. 2-3 um sections were cut and mounted on Poly-L-lysine coated slides. Slides were dried overnight at 37 degree C and dewaxed in xylene and hydrated.
2. Antigen retrieval procedure- The black box was filled 3/4th with citrate buffer and the slide carrier with slides was placed in it. The black box was placed in microwave for 9 mins.
3. Boiling of the solution was observed and the microwave was reset for 6 min and started.
4. The box was removed and cooled under tap water

5. Blocking endogenous peroxidase - Sections were incubated at room temperature in 0.3% H_2O_2 in methanol for 30-45 min and rinsed in running tap water for 5-10 mins and then dipped in distilled water for 1 min.
6. The slides were placed in Tris buffer [only one change for 5 min].
7. Blocking reagent was applied for 5-10 min and excess of it was wipped off.
8. Primary antibodies were applied covering the whole section and incubated at room temperature for 1 hour.
9. Slides were then washed in Triss buffer for 5 minutes.
10. Ultra Vision One HRP polymer covering the whole tissue was applied and incubated at room temperature for 45 mins.
11. Washing was done in TBS buffer [Tris buffer saline] for 5 min [4 changes].
12. One drop of substrate DAB [3, 3- Diaminobenzidine] solution was applied on each slide covering the whole material and incubated for 10-15 mins, then washed in deiodinized water.
13. Hematoxylin was applied for few seconds and washed under running water.
14. Dry and dehydrate in alcohol and incubate for 2 mins.
15. Mounted in DPX [distyrenedibutyl phthalate xylene]

OBSERVATIONS AND RESULTS

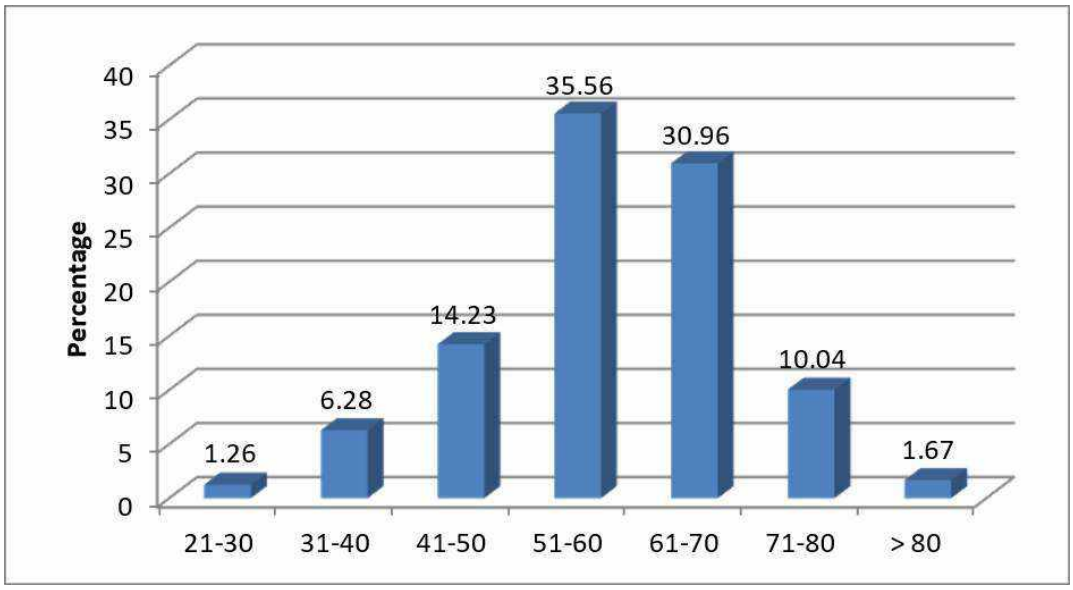
The present study was conducted in the Department of pathology, Dayanand Medical College and Hospital, Ludhiana over a period of 5 years, of which 1.5 years (1st January 2020 to 30th June 2021) were prospective and 3.5 years (1st July 2016 to 31st December 2019) were retrospective.

A total of 71,656 histopathology specimens were received during this study period, out of which, 6976 were hysterectomies, endometrial curettes/biopsies, cervical punch and cone biopsies. Out of these, 239 (3.42%) were malignant uterine tumors.These 239 cases were analyzed with respect to gross and light microscopic findings and categorized as per the 2014 WHO classification for tumors of female genital tract and correlated with immunohistochemical (IHC) findings wherever available.

Table 1.Age wise distribution of the study group

Age group (years)	No. of cases (n=239)	%
21-30	03	1.26
31-40	15	6.28
41-50	34	14.23
51-60	85	35.56
61-70	74	30.96
71-80	24	10.04
>80	04	1.67
Total	239	100.00

Figure 1: Age wise distribution of the study group



The commonest age group affected by uterine malignancies was 51-60 years accounting for 35.56% of the total cases with a mean age of presentation being58.2 years.

Table 2. Distribution of type of specimens

Type of specimens	**No. of cases(n=239)**	**%**
Hysterectomy	186	77.82
Endometrial curettings/biopsies	42	17.57
Cervical punch biopsies	9	3.77
Cervical cone biopsies	2	0.84
Total	239	100.00

Out of the 239 cases, 186 (77.82%) were hysterectomy specimens, 42 (17.57%) were endometrial curetting/biopsies, 9 (3.77%) were cervical punch biopsies and 2 (0.84%) were cervical cone biopsies.

Table 3. Distribution of location of neoplasm

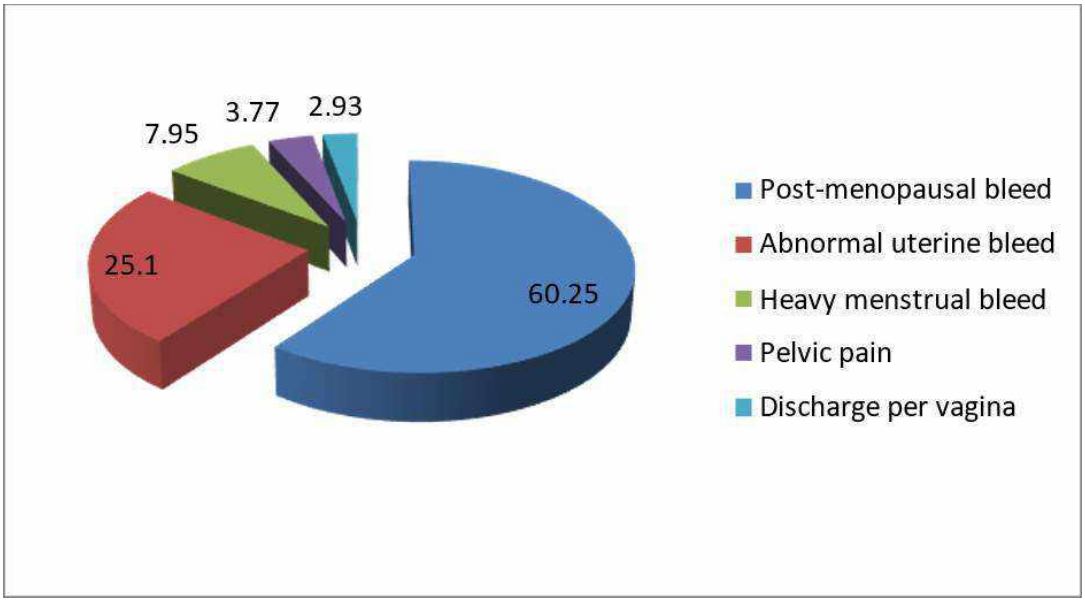
Location of neoplasms	**No. of cases (n=239)**	**%**
Uterine corpus	202	84.52
Uterine cervix	37	15.48
Total	239	100.00

Of the total 239 cases, 202 (84.87%) originated in the uterine corpus and 37 (15.48%) were of the uterine cervix.

Table 4. Distribution of clinical presentation

Symptoms	No. of cases (n=239)	%
Post-menopausal bleed	144	60.25
Abnormal uterine bleed	60	25.10
Heavy menstrual bleed	19	7.95
Pelvic pain	9	3.77
Discharge per vagina	7	2.93
Total	239	100.00

Figure 2: Distribution of clinical presentation



The most common clinical presentation of malignant uterine neoplasms was bleeding in post-menopausal womenseen in 144 (60.25%) of the total 239 cases. 60 (25.10%) cases presented with abnormal uterine bleeding and 19 (7.95%) presented with heavy menstrual bleeding. Pelvic pain was seen in 9 (3.77%) and a history of discharge per vaginum was seen in 7 (2.93%) cases.

Table 5. Spectrum of malignant neoplasms of uterine corpus

Category of malignant neoplasms	No. of cases (n= 202)	%
Epithelial	166	82.18
Mesenchymal	18	8.91
Mixed epithelial and mesenchymal	18	8.91

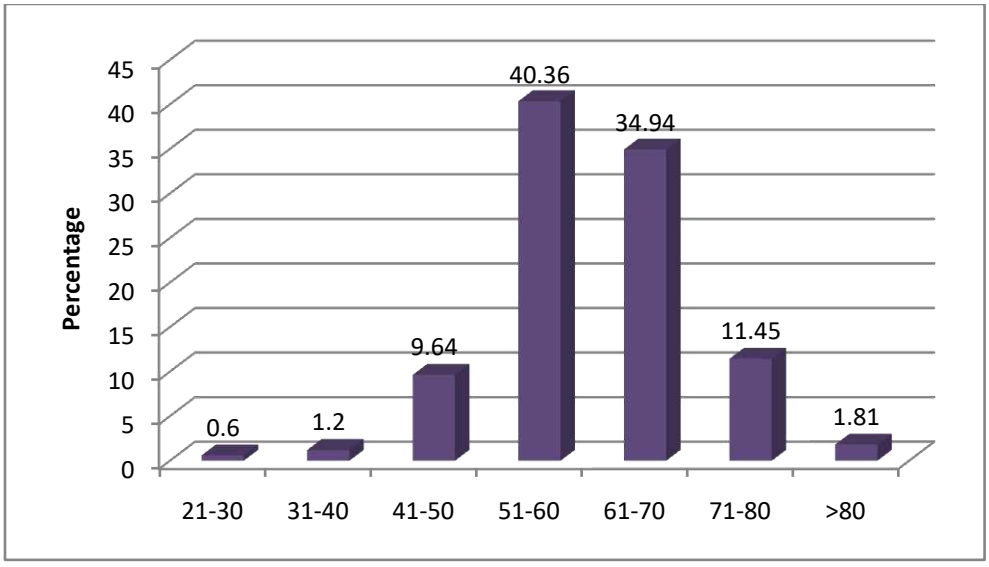
Out of the 202 cases of malignant neoplasms of uterine corpus, 166 were epithelial in origin accounting for 82.18% of the cases. There were 18 cases eachof mesenchymal and mixed epithelial and mesenchymal neoplasms accounting for 8.91% each.

MALIGNANT EPITHELIAL NEOPLASMS OF UTERINE CORPUS

Table 6. Age wise distribution of malignant epithelial neoplasms of uterine corpus

Age Group (Years)	No. Of Cases (n=166)	%
21-30	1	0.60
31-40	2	1.20
41-50	16	9.64
51-60	67	40.36
61-70	58	34.94
71-80	19	11.45
>80	3	1.81
Total	166	100.00

Figure 3: Age wise distribution of malignant epithelial neoplasms of uterine corpus

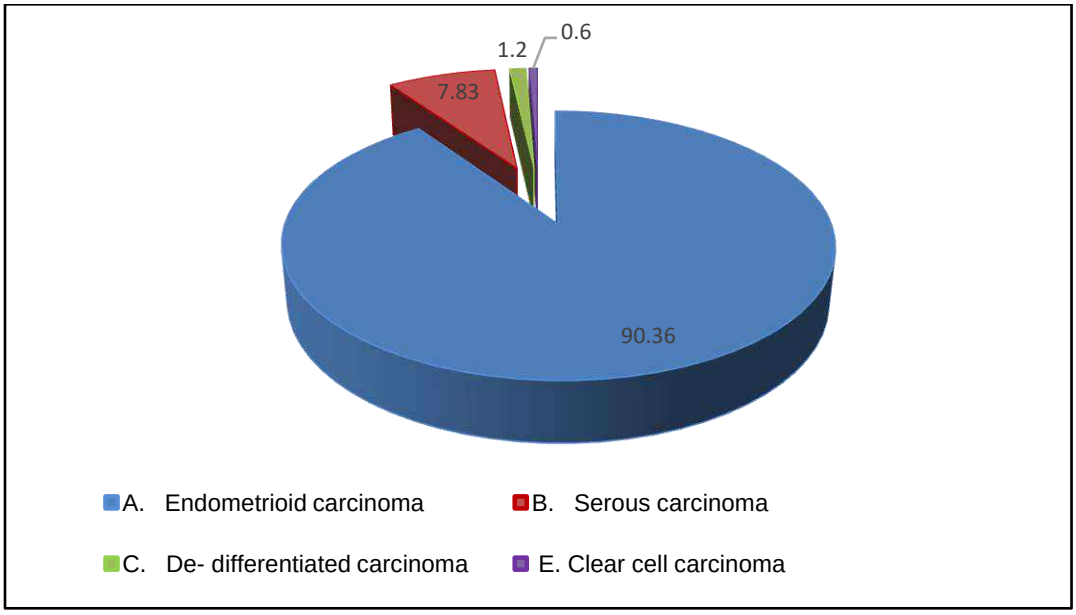


Commonest presenting age group was 51-60 years accounting for40.36% Of the total cases with a mean age of 60.5 years

Table7. Spectrum of malignant epithelial neoplasms of uterine corpus (WHO 2014)

Epithelial	No. Of cases (n=166)	%
A. Endometrioid carcinoma	150	90.36
B. Serous carcinoma	13	7.83
C. De- differentiated carcinoma	2	1.20
E. Clear cell carcinoma	1	0.60

Figure 4: Spectrum of malignant epithelial neoplasms of uterine corpus (WHO 2014)



In our study, the commonest epithelial malignancy of uterine corpus was endometrioid carcinoma accounting for 150 (90.36%) cases. This was followed by 13 (7.83%) cases of serous carcinomas, 2 (1.20%) cases of de-differentiated carcinoma and solitary case of clear cell carcinoma of endometrium.

Table 8. Distribution of type of specimen

Type Of Specimen	Endometrioid	Serous	Clear Cell	De-Differentiated
Hysterectomy	124(82.7%)	6(46.2%)	1(100%)	2(100%)
Endometrial curettings/biopsy	26(17.3%)	7(53.8%)	0	0
	150	13	1	2

Of the 150 cases of endometrioid carcinoma, 124 were hysterectomies and 26 were endometrial curetting/biopsies.

Amongst 13 cases of serous carcinoma, 7 were diagnosed on endometrial curetting/biopsies and 6 on hysterectomy specimens.

Both the cases of de-differentiated carcinoma were diagnosed on hysterectomy specimens. The only case of clear cell carcinoma was diagnosed on hysterectomy.

Table 9. Distribution of tumor size in uterus

Size(cm)	Endometrioid	Serous	Clear Cell	De-Differentiated
< 1	1(0.8%)	0	0	0
1- 5	101(81.5%)	5(83.3%)	1(100%)	1(50%)
>5-10	22(17.7%)	1(16.7%)	0	1(50%)
>10	0	0	0	0
	124	6	1	2

In our study, maximum cases of malignant epithelial neoplasms of the uterine corpus ranged between 1- 5 cm followed by >5-10 cm.

Table 10. Location of tumor in uterus

Location	Endometrioid	Serous	Clear cell	De-differentiated
Confined to fundus and body	43(34.7%)	3(40%)	1(100%)	0
Fundus, body and isthmus	59(47.6%)	3(60%)	0	2(100%)
Fundus, body, isthmus and endocervix	22(17.7%)	0	0	0
	124	6	1	2

In the present study, 59 (47.6%), 3 (60%) and 2 (100%) cases of endometrioid carcinoma, serous carcinoma and de-differentiated carcinoma respectively had a mass involving the fundus, body and extending up to the isthmus of uterus. This was followed by a mass confined to the fundus and body alone of uterine cavity accounting for 43 (34.7%), 6 (60%), 1 (100%) case of endometrioid carcinoma, serous carcinoma and clear cell carcinoma respectively. In 22 (17.7%) cases of endometrioid carcinoma, tumor mass extended from fundus up to the endocervix.

Hence, it was observed in the present study that a mass involving fundus, body and isthmus of uterus was the most common, accounting for 47.6%, 60%, and 100% cases of endometrioid, serous and de-differentiated carcinoma of uterus respectively.

Table11. Extent of tumor invasion of myometrium on gross examination

Extent	Endometrioid	Serous	Clear cell	De-differentiated
Confined to endometrium	-	1(16.67%)	-	-
<1/2 of myometrium	70(56.5%)	1(16.67%)	1(100%)	-
>1/2 of myometrium	54(43.5%)	4(66.67%)	-	2(100%)
	124	6	1	2

In our study, 70 (56.5%) cases of endometrioid carcinoma infiltrated <1/2 of the myometrium. Fifty-four (43.5%) cases infiltrated >1/2 of the myometrium, out of which 1 case also reached upto the serosa.

Amongst serous carcinoma, 4 (66.67%) cases infiltrated >1/2 of the myometrium and only 1 (16.67%) case infiltrated <1/2 of the myometrium.There was one case which presented as a polyp and was confined only to the endometrium.

The only case of clear cell carcinoma infiltrated <1/2 of the myometrium and both the cases of de-differentiated carcinomas infiltrated >1/2 of the myometrium.

So, it was observed that >1/2 of myometrial invasion was more common in serous carcinoma (66.67%) and de-differentiated carcinoma (100%) in comparison to endometrioid carcinoma (43.5%).

In all these cases, the extent of invasion on microscopy corresponded with the findings of gross examination.

Table 12. Distribution of endometrial background changes

Category	Endometrioid (n=150)	Serous (n=13)	Clear Cell (n=1)	De-Differentiated (n=2)
Endometrial hyperplasia without atypia	9(6%)	1(7.7%)	1(100%)	-
Atypical endometrial hyperplasia	14(9.33%)	-	-	-
Senile cystic atrophy	42(28%)	8(61.53%)		1(50%)
Carcinoma arising in endometrial polyp	1(0.67%)	1(7.7%)	-	-
No background endometrial changes	84(56%)	3(23.07%)	-	1(50%)
	150	13	1	2

In the present study, 76(45.7%) out of 166 cases of malignant epithelial neoplasms of uterine corpus showed morphological changes in endometrium. Senile cystic atrophy was the commonest association accounting for 42 (28%) and 8 (61.53%) cases of endometrioid carcinoma and serous carcinoma respectively. It was seen as presence of multiple cystically dilated endometrial glands lined by atrophic epithelium present in a dense fibrous stroma.

Endometrial hyperplasia without atypia seen as an exaggerated proliferation of irregularly shaped and sized endometrial glands with increase in gland to stroma ratio but without significant cytological atypia, was associated with 9(6%) cases of endometrioid and 1 (7.7%) case of serous carcinomas.

Atypical endometrial hyperplasia was seen in 14 (9.33%) cases of endometrioid carcinoma. The diagnosis was made based on presence of increased gland to stroma ratio with little intervening stroma and superimposed features of nuclear atypia which included nuclear enlargement, rounding, loss of polarity and pleomorphism.

There were 2 cases diagnosed as carcinoma arising in an endometrial polyp, 1 being endometrioid carcinoma and the other serous carcinoma.

So, it was observed in the present study that serous carcinomas arose more commonly in a background of senile cystic atrophy (61.53%) of the endometrium, while endometrioid carcinoma was more commonly seen in the background of atypical endometrial hyperplasia (9.33%).

Morphology and Immunohistochemistry

Endometrioid carcinoma: It was the commonest malignant epithelial neoplasm of uterine corpus accounting for 150 (90.36%) cases.Sixty-two (41.3%) cases were within the age group of 51-60 years presenting with post-menopausal bleed in 95 (63.3%) cases. The most common pattern seen was glandular. The lining cells were columnar having inconspicuous nucleoli and moderate amount of cytoplasm. Based on architectural and nuclear grading, 99 (66%) cases were categorized as FIGO grade I in which the solid component was <5% of total tumor area and mild degree of nuclear atypical. It was followed by 38 (25.3%) cases of FIGO grade II in which solid tumor was >5% but <50% and a moderate degree of nuclear atypical. There were 12 cases in which the solid component was >50% of tumor area and the nuclear atypical were marked. However, there was one case in which the architectural grade was II but nuclei showed marked degree of atypical and hence the case was categorized

as FIGO grade III. Hence, there were a total of 13 (8.6%) cases of FIGO grade III. Hundred and nineteen (95.96%) cases belonged to T1 category.

A predominant villoglandular architectural pattern was seen in 6 (4%) cases. Squamous differentiation with presence of squmous morules composed of polygonal squamoid cells having abundant eosinophilic cytoplasm was seen in 3 (2%) cases.

LVSI was seen in 2 (1.3%) cases while perineural invasionwas seen in none. Parametrium was involved only in one case (0.6%). Lymph nodes were involved in 8 (5.3%) cases out of which 5 cases had pelvic lymph node involvement, 2 cases hadpara- aortic lymph node involvement and 1 case had both pelvic and para-aortic lymph node involvement. Adnexal involvement was seen in 4 (2.6%) cases.

IHC was available in 36 cases. Of these 36 cases, ER was done in 28 cases and PR was done in 13 cases, both of which showed diffuse nuclear positivity in all these cases. P53 was done in 18 cases all of which showed patchy or weak nuclear positivity correlating with wild type TP53 mutations. P16 was done in 23 cases, out of which it was patchy positive in 20 cases and diffuse nuclear and cytoplasm positivity in 3 cases which were FIGO grade I, II and III respectively. WT1 was done in 32 cases and was negative in all of them.

Ki-67 was done in 7 cases. Two of these cases were FIGO grade III and had a ki-67 of 90% and 40% respectively. Four cases were of FIGO grade II with Ki-67 ranging from 15%-70% and 1 case was of FIGO grade I with Ki-67 of 30%.

CK7 and CK20 were done in 17 cases, all of which were CK7 positive and CK20 negative. CK 5/6 was found to be positive in areas of squamous morules.

Microsatellite Instability panel was available in 6 cases, out of which 5 were MMR proficient and one case showed loss of MSH2 and MSH6 which was post-menopausal patient presenting with bleeding. The initial diagnosis was made on endometrial curettings which was then followed by

a hysterectomy. Tumor was present in fundus, body, isthmus and reaching up to endocervix with <1/2 of myometrial invasion and was FIGO grade I with <5% solid area.

So, in the present study, it was observed that endometrioid carcinomas of uterine corpus showed a diffuse strong positivity for ER and PR, wild type positivity for p53, patchy positivity for p16 in majority of the cases and a negative WT1. Ki-67 index ranged between 15%-90% which varied according to tumor grade.

Serous carcinoma: There were 13(7.83%) cases of serous carcinoma out which 10 (76.9%) presented within the age group of 61-70 years with a complaint of post-menopausal bleed in 12 (92.3%) cases. All the cases showed a complex papillary architectural pattern with presence of branching papillae and cellular tufting. Seven cases also showed a focal solid and sheeting pattern. The lining epithelial cells were markedly pleomorphic with macronucleoli and conspicuous mitotic activity. Adnexal involvement along with metastasis to pelvic and para-aortic lymph nodes was seen in 1 case (8.3%).

IHC was available in 6 cases all of which showed a diffuse strong nuclear p53 positivity. A very high Ki-67 index ranging from 60% to 85% with a mean Ki-67 of 77.5% was seen. ER was focal positive in 5 cases and negative in 1 case. WT1 was done in 4 cases including the case with adnexal involvement and was negative in all. CK7 positivity and CK20 negativity was seen in 5 cases.

Hence, it was observed in our study that serous carcinomas showed a diffuse strong positivity for p53and a highKi-67 index in all cases along with focal positivity for ER in majority of the cases.

De- differentiated carcinoma: There were 2 (1.20%) cases of de-differentiated carcinoma. Both the cases showed tumor cells arranged in a predominant sheeting pattern with focal glandular pattern with the well differentiated component being endometrioid carcinoma FIGO grade II. Foci of squamous differentiation were also seen in one case. LVSI was

present in both the cases.IHC was available only in 1 case which showed positivity for ER, PR in the well differentiated component and CK, EMA, CK8/18, beta catenin, cyclin D1 and patchy p53 in undifferentiated component. WT1 was negative.

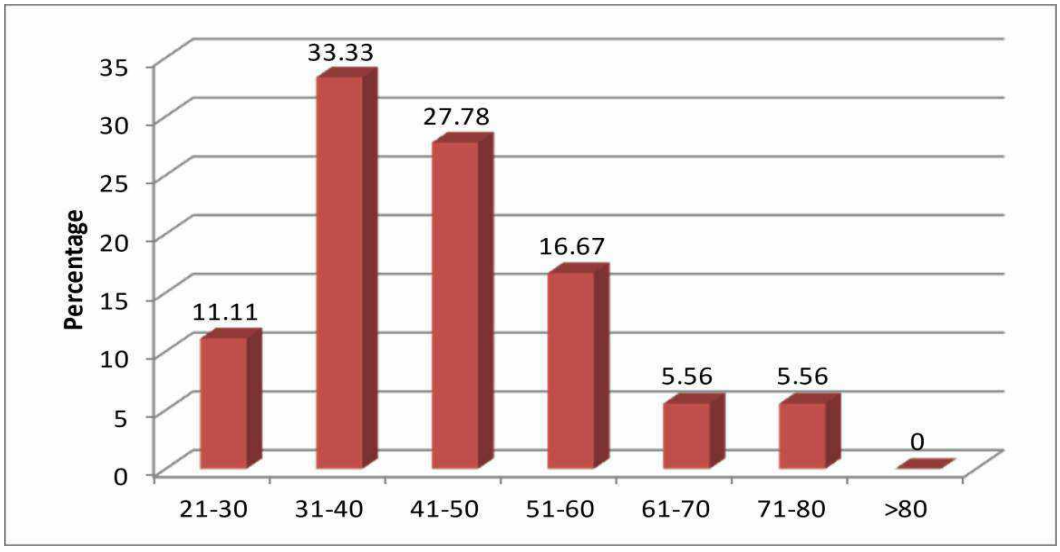
Clear cell carcinoma: There was 1 case (0.60%) of clear cell carcinoma. The tumor cells were arranged in a predominant papillary with focal glandular pattern composed of cells having moderately pleomorphic vesicular nuclei, prominent nucleoli and moderate eosinophilic cytoplasm with clearing and hob nailing at places. Adjacent endometrium showed features of endometrial hyperplasia without atypia.IHC showed positivity for Napsin A. Furthermore, it was negative for ER, WT1, p16 and p53 was weakly positive. Ki-67 was 40%. CK7 was positive and CK20 was negative. Hence correlating the morphology with IHC, a final diagnosis of clear cell carcinoma was given.

MALIGNANT MESENCHYMALNEOPLASMS OF UTERINE CORPUS

Table 13. Age wise distribution malignant mesenchymal neoplasms of uterine corpus

Age group (Years)	No. of cases (n=18)	%
21-30	2	11.11
31-40	6	33.33
41-50	5	27.78
51-60	3	16.67
61-70	1	5.56
71-80	1	5.56
>80	0	0.00
Total	18	100.00

Figure 5: Age wise distribution malignant mesenchymal neoplasms of uterine corpus

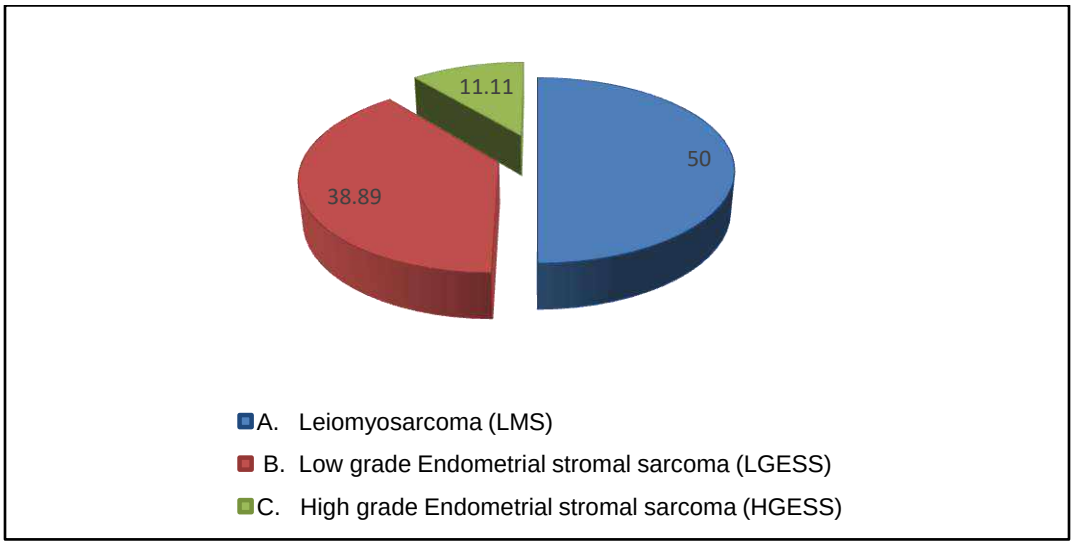


Overall, the commonest presenting age group was 31-40 years accounting for 33.33% of the total cases with a mean age of 44.3 years.

Table 14. Spectrum of malignant mesenchymal neoplasms of uterine corpus (WHO 2014)

Category	No. of cases (n= 18)	%
A. Leiomyosarcoma (LMS)	9	50
B. Low grade Endometrial stromal sarcoma (LGESS)	7	38.89
C. High grade Endometrial stromal sarcoma (HGESS)	2	11.11

Figure 5: Spectrum of malignant mesenchymal neoplasms of uterine corpus (WHO 2014)



In our study, out of the 18 cases of malignant mesenchymal tumors there were 9 (50%) of LMS, 7 (38.89%) cases of low grade and only 2 (11.11%) cases of high grade ESS.

Table 15. Distribution of type of specimen

Type of specimen	Leiomyosarcoma	Endometrial Stromal Sarcoma
Hysterectomy	8 (77.8%)	5 (55.6%)
Endometrial curettings/biopsies	1 (11.1%)	4 (44.4%)
	9	9

Of the 9 cases of Leiomyosarcoma, 8 (77.8%) were diagnosed on hysterectomy specimen and 1 (11.1%) on endometrial curetting/biopsies. Amongst 9 diagnosed cases of endometrial stromal sarcoma, 5 (55.6%) were on hysterectomy specimens and 4 (44.4%) were on endometrial curettings/biopsies.

Table 16. Distribution of tumor size in uterus

Size (cm)	Leiomyosarcoma	Endometrial Stromal Sarcoma
< 1	-	-
1-5	2(25%)	2(40%)
>5-10	4(50%)	3(60%)
>10	2(25%)	-
	8	5

In the present study, it was observed that maximum cases of malignant mesenchymal neoplasm of the uterine corpus ranged between >5- 10 cm accounting for 4 (50%) cases and 3 (60%) cases each of leiomyosarcoma and endometrial stromal sarcoma respectively. This was followed by a tumor size of 1-5 cm accounting for 2 (28.6%, 40%) cases each of leiomyosarcoma and endometrial stromal sarcoma respectively. 2 (28.6%) cases of leiomyosarcoma were >10 cm.

Table 17. Location of tumor in uterus

Location	Leiomyosarcoma	Endometrial Stromal Sarcoma
Confined to fundus and body	1(12.5%)	4(80%)
Fundus, body and isthmus	7(87.5%)	1(20%)
Fundus, body, isthmus and ectocervix	-	-
	8	5

It was observed that 7 (87.5%) cases of leiomyosarcoma and 1(20%) case of endometrial stromal sarcoma involved fundus, body and isthmus of uterus.While only 1 (12.5%) case of leiomyosarcoma and 4(80%) cases of endometrial stromal sarcoma involved fundus and body alone.

Table18. Extent of tumor invasion of myometrium on gross examination

Extent	Leiomyosarcoma	Endometrial Stromal Sarcoma
<1/2 myometrium	1(12.5%)	-
>1/2 myometrium	7(87.5%)	5(100%)
	8	5

In the present study, 7 (87.5%) cases of leiomyosarcoma infiltrated >1/2 of the myometrium. Only one case (14.3%) infiltrated <1/2 of the myometrium. Amongst endometrial stromal sarcoma, all 5 cases infiltrated >1/2 of the myometrium. Hence, in our study we observed that malignant

mesenchymal neoplasms of uterus most commonly infiltrated >1/2 of the myometrium.

In all these cases, the extent of invasion on microscopic examination corresponded with the findings of gross examination.

Morphology and Immunohistochemistry

Leiomyosarcoma: There were 9 cases of uterine leiomyosarcoma. The mean age of presentation was 50.1 years. Pattern of arrangement of tumor cells in these cases was in sheets and fascicles composed of pleomorphic spindled cells in majority of the cases with 4 cases showing epithelioid morphology at places. Presence of diffuse moderate to severe nuclear atypia, coagulative necrosis and mitotic count of > 10/10HPF formed the basis for criteria to classify these cases.

Table19. Morphological findings in uterine leiomyosarcoma

Criteria	**No. of cases (n=9)**	**%**
Nuclear atypia		
a. moderate to severe	9	100.0
b. none	0	-
Coagulative necrosis		
a. present	9	100.0
b. absent	0	-
Mitosis		
a. ≥10/ 10 hpf	7	77.8
b. ≤10/10 hpf	2	22.2

A diffuse moderate to severe nuclear atypia and a coagulative type of necrosis seen as an abrupt transition between the necrotic and viable tumor cells was present in all the cases. Mitotic count per 10 HPF was > 10 in 7 cases and ≤10 in only 2 cases. However, both these cases had

coagulative necrosis along with diffuse moderate to severe nuclear atypia, hence diagnosed as LMS.

Out of the total 9 cases of leiomyosarcoma, IHC was available in 6 cases. SMA was positive in all 6 cases; desmin was positive in 3 and negative in 3 cases respectively. Vimentin was done in 4 cases and was positive in all. Other markers for mesenchymal neoplasms were also done which included CD34 which was done in 4 cases and was negative in all, S100 was done in 2 and was negative in both, CD117 and Bcl2 were done in one case each and were both negative.CD10 was done in 4 cases with focal epithelioid morphology to rule out ESS out of which it was negative in 3 cases and focal positive in one. ER was done in 3 cases out of which it was positive in 2 cases. The one case that was negative for ER was also negative for PR but positive for WT1 and SMA. Ki-67 was done in 4 cases and index ranged from 12%- 80%.

So, it was observed in the present study that leiomyosarcomas were most commonly found to be positive for SMA and vimentin with a high Ki-67 index. However, desmin positivity was observed in only 50% of the cases of LMS.

Endometrial stromal sarcoma: There were 9 cases of endometrial stromal sarcoma which were categorised into low and high grade. The mean age of presentation was 38.6 years. In low grade ESS cases, the tumor cells were arranged as irregular nests and sheets with infiltration of the myometrium in a tongue like projection without an associated stromal reaction. The individual tumor cells exhibited minimal atypia and a low mitotic count was noted.In high grade ESS cases, there was a dual population of round to oval cells along with focal areas of spindled cells having ill-defined cytoplasm. A higher mitotic count of >5/10 HPF was seen.Presence of interspersed arteriole type small vessels with whorling of tumor cells around them was seen in both low- and high-grade cases. Lymphovascular invasion was seen in 2 (22.22%) cases and metastasis to adnexa was seen in only 1 (11.11%) case.

Out of the total 9 cases of endometrial stromal sarcoma, IHC was available in 7 cases.Correlating morphology with IHC findings, a final diagnosis of HGESS was given in 2 cases and 5 cases were diagnosed as LGESS.

Both the cases of HGESS showed a strong cyclin D1 positivity and focal CD10 positivity. ER, PR, desmin and h-caldesmon were negative. SMA was positive in one case.Ki-67 index was high in both, 70% and 95% respectively.

Out of the 5 cases of LGESS, a diffuse CD10 positivity was seen in 4 cases. Out of these 4 cases, there was one case which had a mitosis of >5/10 HPF and a coagulative type necrosis in > 50% of the tumor area, hence was subjected to cyclin D1 which turned out to be negative. ER was positive in all 4 cases and PR was done in only one case which was positive. SMA was focal weak positive in 2 and negative in 2 cases respectively. Desmin was done in 3 cases, out of which, it was focal positive in 2 and negative in one case. In addition, CD117 was also done in 3 cases and was negative in all of them. CD34 and S100 were done in one case and were both negative.Ki-67 index was low in all 4 cases and ranged from 1% to 25%.

In the remaining 1 case, only ER and PR were done which were both positive. In this case a diagnosis of LGESS was made correlating with typical morphological features present on histological examination.

Maximum cases of malignant mesenchymal neoplasms of uterine corpus belonged to T1 category accounting for 10 (76.9%) cases.

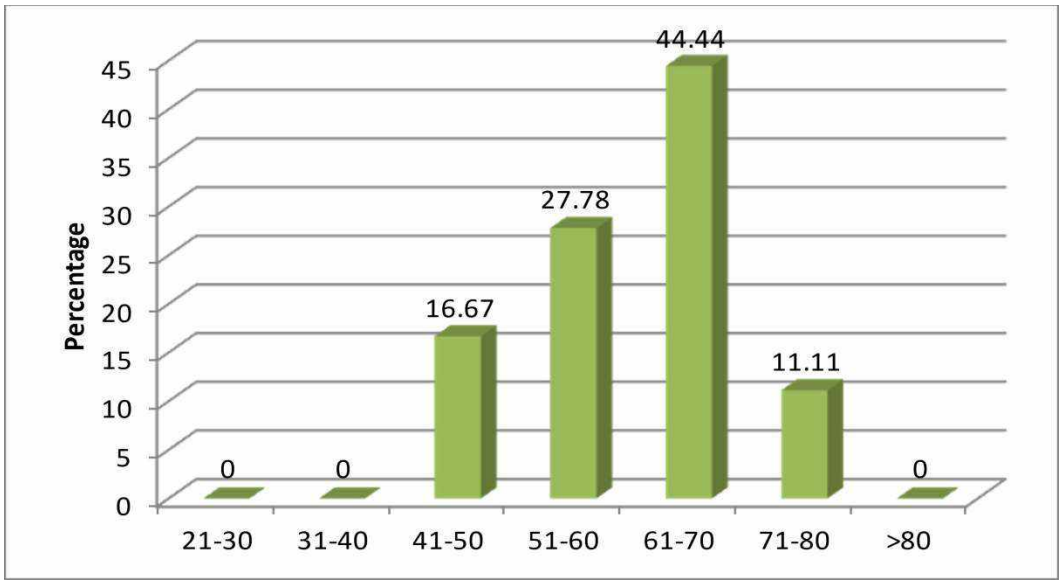
Hence, it was observed in the present study that low grade endometrial stromal sarcomas were most commonly positive for CD10 along with ER and PR with a low ki-67 index. While high grade endometrial stromal sarcomas were consistently positive for cyclin D1 inhigh grade areas and focal positive for CD10 in low grade areas.

MALIGNANT MIXED EPITHELIAL AND MESENCHYMALNEOPLASMS OFUTERINE CORPUS

Table20. Age wise distribution of malignant mixed epithelial and mesenchymal neoplasms of uterine corpus

Age group (years)	No. of cases (n=18)	%
21-30	0	0.00
31-40	0	0.00
41-50	3	16.67
51-60	5	27.78
61-70	8	44.44
71-80	2	11.11
>80	0	0.00
Total	18	100.00

Figure 6: Age wise distribution of malignant mixed epithelial and mesenchymal neoplasms of uterine corpus



Commonest presenting age group was 61-70 years accounting for 44.44% of the total cases with a mean age of 60.7 years.

Spectrum of malignant mixed epithelial and mesenchymal neoplasms of uterine corpus (WHO 2014)

In our study, all the cases of malignant mixed epithelial and mesenchymal tumors of uterus were of carcinosarcoma/Malignant mixed epithelial and mesenchymal tumor (MMMT).

Table21. Distribution of type of specimens

Type of specimen	No. of cases (n=18)	%
Hysterectomy specimen	14	77.8
Endometrial Curetting/biopsies	4	22.2
	18	100.0

Of the 18 diagnosed cases of carcinosarcoma, 14 (77.8%) werehysterectomy specimen and 4 (22.2%) were endometrial curetting/biopsies.

Table22. Distribution of tumor size in uterus

Size (cm)	MMMT/Carcinosarcoma	%
< 1	0	0.0
1-5	4	28.6
>5-10	10	71.4
>10	0	0.0
	14	100.0

In our study, maximum cases of carcinosarcoma of the uterine corpus ranged between >5- 10 cm accounting for 10 (71.4%) cases. This was followed by 1- 5cm accounting for 4 (28.6%) cases.

Table23. Location of tumor in uterus

Location	MMMT/Carcinosarcoma	%
Confined to fundus and body	3	21.4
Fundus, body and isthmus	7	50.0
Fundus, body, isthmus and endocervix	4	28.6
	14	100.0

In the present study, 7 (50%) cases of carcinosarcoma had a mass involving the fundus, body and extending up to the isthmus. There were 4 (28.6%) cases in which a mass present in the fundus, body, isthmus and also extending to the endocervix. In the remaining 3 (21.4%) cases mass was confined to the fundus and body alone of uterine cavity.

Hence, it was observed that 50% cases of malignant mixed epithelial and mesenchymal tumours in our study involved fundus, body and isthmus of uterus.

Table24. Extent of tumor invasion of myometrium on gross examination

Location	MMMT/Carcinosarcoma	%
<1/2 myometrium	3	21.4
>1/2 myometrium	11	78.6
	14	100.0

In the present study, it was observed that11 (78.6%) cases ofcarcinosarcoma infiltrated >1/2 of the myometrium, 2 of which also reached up to the serosa and only 3(21.4%) cases infiltrated <1/2 of the myometrium. These findings corresponded with the microscopic findings.

Morphology and Immunohistochemistry

All the 18 cases of mixed epithelial and mesenchymal neoplasms were Malignant mixed Mullerian tumor/Carcinosarcoma. All the cases were composed of a biphasic malignant epithelial component seen as variably sized glands lined by pleomorphic cells with vesicular nuclei, prominent nucleoli and moderate amount of cytoplasm and a malignant mesenchymal component seen as a high-grade sarcoma with tumor cells arranged in fascicles and sheets of spindle cells.

In 3 (16.66%) cases, the epithelial component was of endometrioid carcinoma seen as cell arranged in the form of glands lined by stratified columnar cells having oval vesicular nuclei exhibiting moderate pleomorphism. In 1 (5.55%) case the epithelial component was of serous carcinoma which was seen as tumor cells arranged in sheets and focal papillary configuration.

In 3 cases, the mesenchymal component showed rhomboid differentiation seen as presence of large cells with abundant eosinophilic cytoplasm and an eccentrically placed nucleus.

Out of the total 18 cases of carcinosarcoma, heterologous elements were seen in 7 (38.88%) cases, out of which 3 cases had osteoid and 4 cases each had chondroid elements respectively.

Parametrium was involved in 2 (14.28%) cases. Metastasis to pelvic lymph nodes was seen 4 (28.57%) cases and metastasis to adnexa was seen in only 1 (7.1%) case. Maximum cases belonged to T1 category accounting for 12 (66.6%) cases.

Out of total 18 cases, IHC was available in 9 cases of carcinosarcoma. The epithelial component was positive for CK in all 9 cases. Myogenin was seen focal positive in the mesenchymal component in one case and negative in 2 cases. Out of the 3 cases with rhomboid differentiation, IHC was available in 1 case which showed myogenin positivity in the mesenchymal component.

The one case with epithelial component seen as serous carcinoma showed diffuse strong positivity for p53 and focal positivity for p16 in the epithelial component along with CK, CK7 and PAX8. However, ER, WT1 and CK20 were all negative. Ki- 67 was 90%.

ER was done in 6 cases out of which, epithelial component was positive in 4 cases and negative in 1 but PR showed positivity in this case.

WT1 was done in all 9 and showed focal positivity in epithelial component in 1 case, and was negative in the remaining 8 cases. Vimentin was done in 7 cases which showed diffuse positivity for mesenchymal component and focal positivity for epithelial component in all cases. SMA was done 3 cases out of which, mesenchymal component was focal positive in one case and negative in 2 cases. Desmin was done in 4 cases out of which, mesenchymal component was positive in 2 cases and negative in 2 cases. S100, cyclinD1 and p63 were negative in all cases.

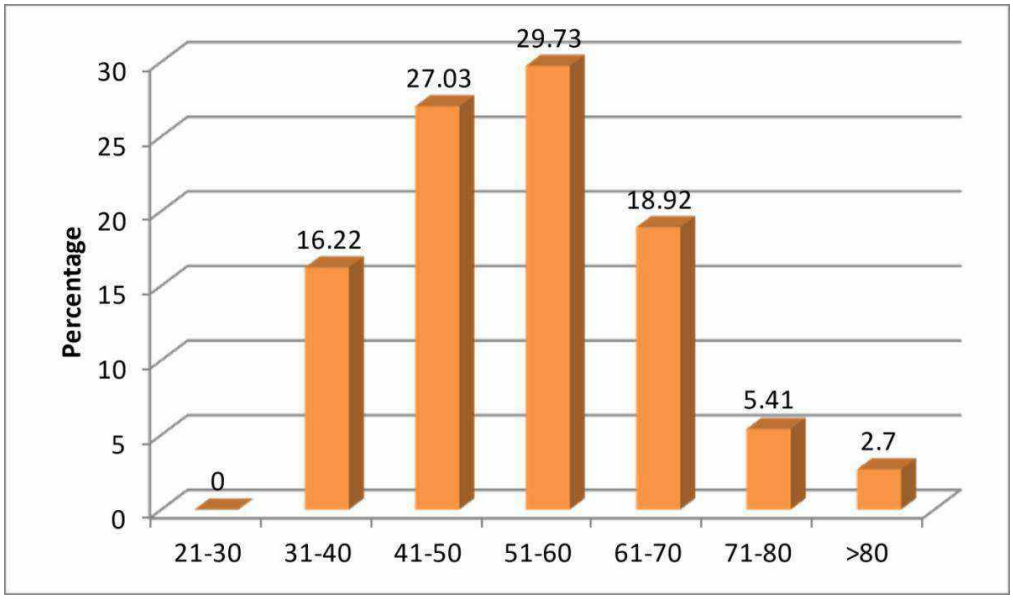
Hence, it was observed in the present study, that the epithelial component of carcinosarcomas was most commonly positive for CK, ER, PR and CK7 while the mesenchymal component was most commonly positive for vimentin, desmin and SMA. Myogenin was positive in areas of rhabdoid differentiation. However, there is no definitive role of IHC in MMMT.

MALIGNANT NEOPLASMS OF UTERINE CERVIX

Table25. Age wise distribution of malignant neoplasms of uterine cervix

Age group (years)	No. Of cases (n=37)	%
21-30	0	0.00
31-40	6	16.22
41-50	10	27.03
51-60	11	29.73
61-70	7	18.92
71-80	2	5.41
>80	1	2.70
Total	37	100.00

Figure 8: Age wise distribution of malignant neoplasms of uterine cervix

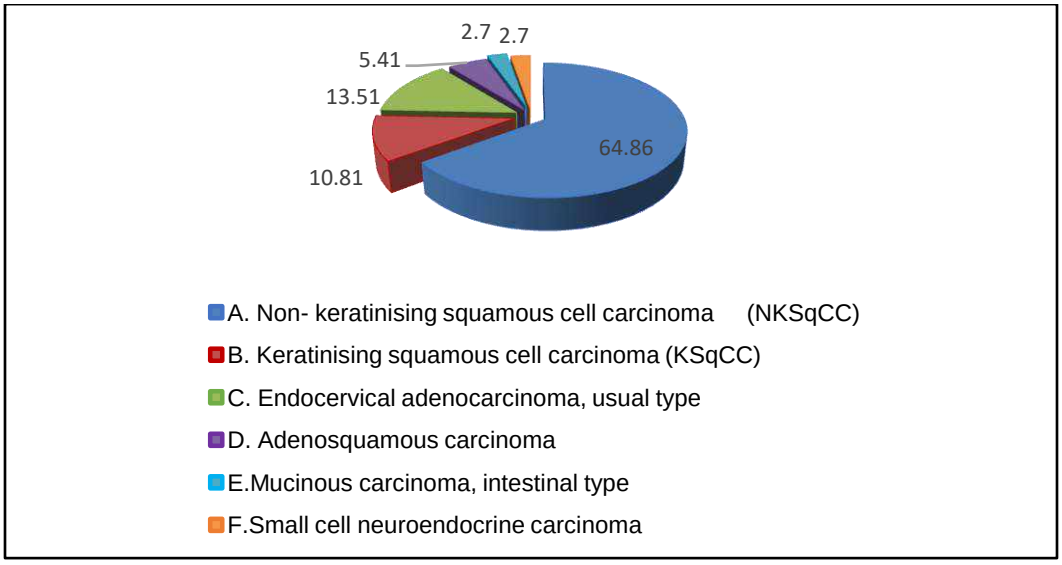


Commonest presenting age group was 51-60 years accounting for 29.73% of the total cases with a mean age of 53.5 years.

Table26. Spectrum of malignant neoplasms of uterine cervix (WHO 2014)

Category	No. Of cases (n= 37)	%
A.Non- keratinising squamous cell carcinoma (NKSqCC)	24	64.86
B.Keratinising squamous cell carcinoma (KSqCC)	4	10.81
C.Endocervical adenocarcinoma, usual type	5	13.51
D.Adenosquamous carcinoma	2	5.41
E.Mucinous carcinoma, intestinal type	1	2.70
F.Small cell neuroendocrine carcinoma	1	2.70
Total	37	100.00

Figure 7: Spectrum of malignant neoplasms of uterine cervix(WHO 2014)



In our study, there were maximum cases of non-keratinising squamous cell carcinoma cervix (NKSqCC) accounting for 24 (64.86%) cases. This was followed by 5 (13.51%) cases of endocervical adenocarcinoma

(ECC), 4 (10.81%) cases of keratinizing squamous cell carcinoma (KSqCC) and 2 (5.41%) cases of adenosqumaous carcinoma. There was one case each of mucinous carcinoma and small cell neuroendocrine carcinoma of cervix (SCNEC).

Table27. Distribution of type of specimen

Type of specimen	**No. Of cases (n=37)**	**%**
Hysterectomy	26	70.03
Cervical punch biopsy	9	24.3
Cervical cone biopsy	2	5.4
	37	100.0

Of the 37 diagnosed cases of malignant neoplasms of uterine cervix in our study, 26 (70.03%) were hysterectomy specimens, 9 (25.0%) werecervical punch biopsies and 2 (5.6%) cervical cone biopsies were received.

Table 28. Distribution of location of tumor

Extent		NKSqCC (n=16)	KSqCC (n=3)	ECC (n=3)	Adenosquamous (n=2)	Mucinous carcinoma (n=1)	SCNEC (n=1)
Confined to cervix	Grossly not visible	4(25.0%)	1(33.33%)	2(66.67%)	-	-	-
	Grossly visible	3(18.8%)	1(33.33%)	-	1(50%)	-	1(100%)
Cervix and isthmus		4(25.0%)	-	1(33.33%)	-	1(100%)	-
Cervix, isthmus and body of uterus		5(31.2%)	1(33.34%)	-	1(50%)	-	-

In the present study,4 (25.0%), 1 (33.33%) and 2 (66.67%) cases of NKSqCC, KSqCC and endocervical adenocarcinoma respectively, had no growth on gross examination and were diagnosed on microscopic examination. The indication for hysterectomy in these cases was complaints of persistent bleeding per vaginum.

Of the remaining 19 cases, maximumcases of NKSqCC had a growth in the cervix and involving the isthmus with an extension upto body of the uterus accounting for 5 (31.2%) cases. This was followed by 4 (25.0%) cases having a growth in the cervix with extension upto isthmus and 3 (25.1%) cases hada growth confined only to the cervix.

One case each of KSqCC and adenosquamous carcinoma had a growth in the cervix and involved the isthmus with an extension upto body of the uterus and as a growth confined only to the cervix respectively.

One case each of endocervical adenocarcinoma and mucinous carcinoma presented as a growth in the cervix with extension upto isthmus.

The only case of small cell neuroendocrine carcinoma had a growth confined to the cervix. So, it was observed that a growth in the cervix with

extension upto isthmus and body of the uterus was most common accounting for31.2%, 33.34% and 50% cases each of NKSqCC, KSqCC and adenosquamous carcinoma of cervix respectively.

Table 29. Distribution of tumor size in uterus

Size(cm)	NKSqCC (n=16)	KSqCC (n=3)	ECC (n=3)	Adenosquamous (n=2)	Mucinous carcinoma (n=1)	SCNEC (n=1)
< 1	4(25.0%)	1(33.33%)	2(66.67%)	-	-	-
1- 5	11(68.8%)	2(66.67%)	1(33.33%)	2(100%)	1(100%)	1(100%)
>5- 10	1(6.3%)	-	-	-	-	-
>10	-	-	-	-	-	-

Itwas observed in the present study, that of the 19 cases with a growth on gross examination, maximum cases of malignant neoplasm of the uterine cervix ranged between 1- 5 cm accounting for 11 (68.8%) cases of NKSqCC, 2 (66.67%) cases of KSqCC, both (100%) cases of adenoquamous carcinoma and one case each of endocervical adenocarcinoma, mucinous carcinoma and small cell neuroendocrine carcinoma. Maximum cases belonged to T1 category accounting for 25 (96.1%) cases of malignant uterine cervix.

Morphology and Immunohistochemistry

Squamous Cell Carcinoma: Non-keratinizing squamous cell carcinoma was the commonest tumor amongst malignant neoplasms of the cervix accounting for 24 (66.67%) cases. Majority of the patients were >50 years old and presented with the complaints of bleeding per vaginum. Tumor was composed of polygonal squamous cells arranged in sheets and nests. These cells had a large round nucleus with a conspicous nucleoli and

moderate to abundant cytoplasm. No keratin pearls were seen in any of the case.LVSI and parametrial involvement was seen in 1 (4.16%) case each.IHC was available in 1 case which showed a diffuse strong positivity for p16 and p40.There were 4 cases of Keratinizing squamous cell carcinoma which showed keratin pearls.IHC was available in 1 case which showed a diffuse strong positivity for p16 and p40.

Endocervical Adenocarcinoma, usual type: There were 5 (13.89%) cases, majority presenting in postmenopausal women with complaints of BPV. All the cases showed tumor cells arranged in glandular and papillary architecture. The lining tumor cells showed nuclear elongation, hyperchromasia with psuedostratification. Metastasis to pelvic lymph nodes was seen in 1(20%) case.

IHC was available in 3 cases all of which were diffuse strong positive for p16.ER was negative in 2 cases but focal positive in 1 case. However, that case was negative for vimentin hence eliminating endometrioid carcinoma. WT1 was negative in all 3 cases. P53 was done in 2 of these cases and was negative in both. Ki- 67 was done in only one case and was 90%.

Adenosquamous carcinoma: There were 2 cases of adenosquamous carcinoma of cervix both presenting in perimenopausal women with history of DPV and AUB respectively. Tumor cells were arranged in nests and sheets.Individual tumor cells had a pleomorphic vesicular nuclei, prominent nucleoli and moderate amount of cytoplasm. Individual cell keratinization was seen. Also identified were areas having presence of back-to-back arranged glands lined by cells exhibiting nuclearhyperchromasia and stratification. Overlying stratified squamous epithelium showed features of carcinoma in situ in 1 case.

Mucinous Carcinoma: A solitary case of mucinous carcinoma was of intestinal type presenting in a 70 years old female with complaints of postmenopausal bleed. The tumor cells were arranged in glandular configuration and showed goblet cells along with extracellular pools of mucin.

Small cell neuroendocrine carcinoma: In a solitary case of small cell neuroendocrine carcinoma, the female was 43 years old presenting with complaints of AUB. The tumor cells were arranged in sheets, having a small round hyperchromatic nucleus with scanty cytoplasm and nuclear moulding. LVSI, brisk mitosis and involvement of bilateral parametrium were noted. Immunohistochemistry correlated with the histological findings. Chromogranin was focal positive and both CD56 and NSE were weak positive. Synaptophysin however was negative. Furthermore, CK showed a dot like positivity whereas LCA and p40 were both negative.

DISCUSSION

Cancers of the female genital tract are amongst the most common cancers in women and hence an important public health issue. As a result of lack of awareness, variable pathology, and dearth of proper screening facilities in developing countries such as India, most women report at advanced stages, thus affecting the prognosis and clinical outcome adversely. Histopathological examination is still the gold standard test to diagnose and rule out malignancy and compulsory for all the surgical specimens.

The present study was a prospective and retrospective study on the histomorphological spectrum of malignant uterine neoplasms of the specimens received in the Department of Pathology, Dayanand Medical college & Hospital, Ludhiana over a period of 5 years (3.5 years retrospective from 1st July 2016 to 31st December 2019 and 1.5 years prospective from 1st January 2020 to 30th June 2021). During this period 239 cases of malignant uterine neoplasms were analyzed with respect to gross and light microscopic findings and categorized as per the 2014 WHO classification for tumors of female genital tract and correlated with immunohistochemical (IHC) findings wherever available.

A total of 71,656 histopathology specimens were received during this study period, out of which, 6976 were hysterectomies, endometrial curettes/biopsies and cervical punch and cone biopsies. Out of these, 239 (3.42%) were malignant uterine tumors.Similar findings were observed by Mandakini B. Tengli et al[51] and Gupta et al[52] with malignant uterine tumors accounting for 3.34% and 2.2% of the cases in their studies respectively.Uterine malignancies typically affect postmenopausal women. Thecommonest age group affected by uterine malignancies in our study was observed to be 51-60 years with a mean age of presentation being 58.2 yearsand bleeding being the commonest clinical presentation in these women. Mustaqueem et al[53] and Binu et al[54] reported similar

findings with maximum cases in 6th decade presenting most commonly with bleeding.

Hysterectomy is the most commonly performed gynecological surgical procedure and provides the whole uterus and cervix with associated pathology as observed by PrathyushaNakka et al[55] and Harshal A. Patilet al.[56] This is in accordance with the present study where 77.82% i.e 186/239 cases were diagnosed on hysterectomies.Hysterectomy helps in adequate sampling of the required and suspected areas and thus helps in diagnosis of various lesions without any error of sampling.

There were 202(84.52%) casesof malignant uterine corpus tumors and 37 (15.48%) cases of malignant uterine cervix tumorsin this study. Momtahen et al(2009)[57] reported 24.9% cases of uterine corpus cancers and 19.6% cases of uterine cervical cancers in his study.Vinh-Hung et al(2007)[58] also observed an overall declining incidence of cervical cancer in his study.However, the pattern of malignancy in our study differs from Mathur et al[59] who found the commonest female genital tract malignancy to be cancer of uterine cervix as did Basile et al[60] and Hanoon et al.[61]. The declining rates of cervical cancer in our study can partly be explained by available HPV vaccines in urban areas, affordable and effective methods for early detection through pap smear screening and treatment of precursor lesions.

Malignant epithelial tumor, arising in the endometrial is the most common malignant tumor of the female genital system which was observed in our study as well with 166 (82.18%) cases of malignant tumors of uterine corpus being epithelial in origin and 8.91% cases each of mesenchymal and mixed epithelial and mesenchymal tumors. These findings are in concordance with most of the published studies in the literature. Cameselle-Teijeiro JF et al[62] observed in his study of 429 cases,93.9% were epithelial and only 4.6% were mesenchymal. Similarly, Binu et al[54] observed 81.81% tumors in his study were epithelial in origin. Ueda et

al[63] also found 91.6% cases to be epithelial and only 8.4% to be mesenchymal in origin in his study.

MALIGNANT EPITHELIAL NEOPLASMS OF UTERINE CORPUS

In the present study, distribution of malignant epithelial tumors of the uterine corpus was found to be:- endometrioid carcinoma (150,90.36%), serous carcinoma (13,7.83%), de-differentiated (2,1.20%) and clear cell carcinoma (1,0.60%) with 51-60 years being the most common age group at presentation. Similar results were observed by PrathyushaNakka et al [55] with the most common age group at presentation between 50 to 60 years and endometrioid carcinoma being the most common malignant neoplasm. Imrana Tanvir et al[64] studied 52 cases, out of which the most common malignant neoplasm was endometrioid carcinoma and the most common age group at presentation being 51–60 years. Present study varies from Cameselle-Teijeiro et al[62], in which out of 429 cases, commonest age group at presentation was 61–70 years.But the most common malignant neoplasm being endometrioid carcinoma same as in the present study. In Bohiltea et al[65] study, out of 826 cases most common neoplasm was endometrioid carcinoma with the most common age group at presentation being 60–65 years.

Endometrioid carcinoma

Out of the 150 cases of endometrioid carcinoma, 124 were hysterectomies and 26 were endometrial curettings/biopsies. In the present study, maximum (70/124, 56.5%) cases infiltrated <1/2 of the myometrium making it the most common presentation with a mass involving the fundus and body of the uterus with extension upto the isthmus.C. Merisio et al [66] made similar observations with 92% (25/27) cases infiltrating <1/2 of the myometrium and so did Nofech-Mozes et al[67] with 424/733 (57.8%) cases of endometrioid carcinoma infiltrating <1/2 of the myometrium.In all our cases, the extent of infiltration on gross and microcscopic examination were in concordance. Larson et al[68] in his study found the association between gross invasion and microscopic invasion to be highly significant

(P < .001) as the estimated depth of gross myometrial invasion correctly predicted the microscopic depth of myometrial invasion on permanent histopathologic sections in 90.3% cases in his study.

Endometrial polyps are mostly benign in origin, although malignancy has been reported in these polyps. There was 1case of endometrioid carcinoma arising in an endometrial polyp accounting for 0.67% which is in accordance with Santos et al[69] who found only seven cases (0.53%) of malignant endometrial polyps in a total of 1333 polyps. Similarly, Shushan et al[70] in his study including 300 endometrial polyps found only 4 were malignant (1.3%).

In the present study, the most common pattern in endometrioid carcinoma was glandular. A predominant villoglandular architectural pattern was seen in 6 (4%) cases and squamous differentiation was seen in 3 (2%) cases. This is discordant with findings made by Ambros et al[71] in his study where 44 (31%) of the 142 cases and Zaino et al[72] where 37 (60.6%) of the 61 cases that formed the study sample, had a villoglandular differentiation. The difference in distribution can be attributed to the smaller sample size from the present study.

Based on architectural and nuclear grading, maximum cases of endometrioid carcinoma were categorized as FIGO grade I accounting for 99 (66%), followed by 38 (25.3%) cases of FIGO grade and 13 (8.6%) cases of FIGO grade III in our study. These findings were in concordance with majority of the studies. Berretta et al[73] indicated 64 cases (43.5%) Grade I, 66 (44.9%) Grade II and 17 (11.6%) Grade III cases amongst endometrioid carcinomas. Hashmi et al[50] applied FIGO grading to 22 cases of endometrioid carcinoma, 50% (11/22) cases were Grade I, 40.91% cases were Grade II (9/22) and the rest were Grade III (9.09, 2/22).

In the present study, lymphovascular invasion (LVSI) was seen in only 2/124 (1.3%) cases with nodal metastasis in 8/124 (5.3%) cases.This finding is in acceptance with findings made by O'Brien et al[74] where of the

41 patients of endometrioid carcinoma, only 5 (12%) were found to have LVSI. Similarly, in Moatasim et al[75] study, out of 70 cases of endometrioid carcinoma, LVSI was noted in only 11 (34.4 %) cases. Berretta et al[73] also reported among 147 patients, 89.1% had no nodal metastases. Rate of nodal metastasis of only 0.8% (3/389) was observed by Milam et al[76] similar to our study.Adnexal involvement in present study was seen in only 4 (2.6%) cases.This is in discordance with Conelle et al[77] who observed, out of the 382 cases reviewed, 40 (10.5%) had adnexal involvement. However, these patients also had high rates LVSI and additional sites of extra uterine disease which was not the case in present study.

Atypical hyperplasia carries a greater risk of cancer progression compared with hyperplasia without cytologic atypia as was the case in the present study. Of the 150 cases of endometrioid carcinoma, the adjacent endometrium showed features of atypical endometrial hyperplasia in 14 (9.33%) cases and endometrial hyperplasia without atypia in only 09 (6%) cases. These findings are consistent with Kurman et al[78] with only 2 (1.6%) of 122 patients in his study with hyperplasia without atypia progressing to carcinoma compared with 11 (23%) of women with atypical hyperplasia. Widra et al[79] also reported in his study 12/24 (50%) cases of atypical endometrial hyperplasia had co-existent carcinoma opposed to none of endometrial hyperplasia without atypia cases.

Immunohistochemistry has a role in understanding tumor biological behavior and help in individual treatment strategies. Most appropriate markers for confirming the diagnoses of endometrioid carcinoma include ER, PR, p53, WT1, and Ki67. The present study, showed a diffuse strong positivity for ER and PR, wild type positivity for p53 in majority of the cases and a negative WT1. This is in concordance with most studies like Nayar Musfera Abdul Masjeed et al[80], JJ Wei et al [81] and Darvishian et al[82] all of which observed a strong ER and PR with wild type positivity of p53 in endometrioid carcinoma.

Microsatellite Instability panel was available in 6 cases in this study, out of which 5 were MMR proficient and one case showed loss of MSH2 and MSH6 which was a postmenopausal woman with FIGO garde I endometrioid carcinoma. These findings are similar to a study done by J.C. Watkins et al[83] where 4 cases (1.7%) displayed MSH2 and MSH6 deficiency by IHC of which 3 were of endometrioid type, grade 1 with ages above 50 years. Similarly, combined MSH2 and MSH6 loss was found in only 3 of total 20 cases showing loss of MMR in a study done by Stelloo et al.[84] Accurate identification of MMR-deficiency is important to identify patients with a higher risk of recurrence.

Ki-67 index ranged between 15%-90% which varied according to tumor grade.Similar findings were seen by Nayar Musfera Abdul Masjeed et al[80] where Ki-67 index increased from 22.52% to 40% as the grade increased.

Serous carcinoma

Amongst 13 cases of serous carcinoma in the present study, 7 were diagnosed on endometrial curetting/biopsies and 6 on hysterectomy specimens. Maximum cases (4/6,66.67%) infiltrated >1/2 of the myometrium with 60% cases involving the fundus, body and also extending upto isthmus of the uterine cavity.On histology, all cases showed a complex papillary architectural pattern with presence of branching papillae and cellular tufting. Lobo FD et al[85] made similar findings in his study which included 8 cases of endometrial serous carcinoma, 70% of which had >1/2 myometrial invasion and a complex papillary architecture. Hashmi et al[50]also reported similar findings with 9/13 (69.2%) cases having >1/2 myomterial infiltration and a diffuse growth of tumor with vague papillary configuration.Adnexal involvement along with metastasis to pelvic and para-aortic lymph nodes was seen in 1 case (8.3%) which was negative for WT1 on IHC in the present study. Adnexal involvement was seen 3 (2.31%) cases in a study by Hashmi et al[50] with 5 cases also showing nodal metastasis.

In the present study, serous carcinomas arose more commonly in a background of senile cystic atrophy (8/13, 61.53%). These findings were similar to majority of the studies such as M.E Sherman et al.[86] In his study, the adjacent endometrium was atrophic in 35/38 (92%) cases and endometrial hyperplasia was seen only in 5% case. Similarly, R. Idrees et al[87] also found the background endometrium to be atrophic in all four cases (100%) in his study.

There was a solitary case of serous carcinoma arising in an endometrial polyp in the present study.McCluggage[88] made similar findings depicting only 2 cases of uterine serous carcinoma arising in a polyp in his study.This shows that uterine serous carcinoma may rarely arise in benign endometrial polyps without myometrial infiltration.

The molecular changes of p53 mutation in 80–90% of serous carcinomas is reflected in p53 immunohistochemistry, which typically shows a diffuse and intense nuclear staining pattern involving almost all tumor cells. In our study too, diffuse strong positivity for p53 was seen in all the 6 cases subjected to IHC. These findings are in concordance with studies byHashmi et al[50] and S. Kounelis et al[89], both showed a significant association between p53 overexpression and serous carcinoma. In addition, all cases in the present study showed a high Ki-67 index which was similar to the findings made by Nayar Musfera Abdul Masjeed et al[80] Zidan AA et al[90] and Stoion SC et al[91], all of which concluded a high mean value of Ki-67 indexfor uterine serous carcinomas in their studies.

De-differentiated carcinoma

Both cases of de-differentiated carcinoma in the present study were diagnosed on hysterectomy specimen presenting as a mass located in the fundus and body of the uterus along with an extension upto isthmus, infiltrating >1/2 of the myometrium. On microscopy both had a predominant undifferentiated component with a focal well differentiated component of endometrioid carcinoma FIGO grade II. On IHC, positivity for ER, PR in the well differentiated component and CK, EMA, CK8/18,

cyclin D1 and patchy p53 in undifferentiated component was noted. These findings are very similar to those explained by Yokomizo et al[92] in his case report on 3 patients, 2 of which had infiltration of>1/2 of myometrium, extending upto isthmus and an undifferentiated component comprising 90% and 60% respectively of the total tumor area. The well-differentiated component was of endometrioid grade I type. IHC results were similar to those in our case.

Clear cell carcinoma

There was a solitary case of CCC in the present study, diagnosed on hysterectomy specimen. The tumor was confined to the fundus and body of the uterus infiltrating <1/2 of the myometrium. The tumor cells were arranged in a predominant papillary with focal glandular pattern with clearing and hobnailing at places. Similar findings were explained by Fadare et al[93] and Abeler and Kjorstad[94] in their clinic pathological analysis on 50 and 66 cases respectively of clear cell carcinomas.Adjacent endometrium showed features of endometrial hyperplasia without atypia. NapsinA positivity on IHC acted as a diagnostic tool in the present study. This is similar to the study by Fatemeh Nili et al[95], in which Napsin A was positive in 83% cases of CCC and in none of the cases with non-CCC's, hence proving a specificity of 100% and sensitivity of 83%.

MALIGNANT MESENCHYMAL NEOPLASMS OF UTERINE CORPUS

Compared to epithelial uterine malignancies, malignant uterine tumors of mesenchymal origin are rare. Within the group of uterine sarcomas, leiomyosarcomas and low-grade endometrial stromal sarcomas by far predominate as the most frequent which was also observed in this study with 9 (50%) cases of LMS, 7 (38.89%) cases of low grade ESS and, 2 (11.11%) cases of high grade ESS.El-Khalfaoui et al[96] and Ishidera et al[97] also reported 60% and 62.5% cases respectively of LMS making it the commonest mesenchymal malignancy in their studies.Maximum number of patients were within the age group of 31-40 years with a mean

age of 44.3 years in our study similar to S. A. Barquet-mu noz et al[45] who reported a mean age of 48.1 years in his study.

Leiomyosarcoma

Most uterine LMS are large solitary lesions with irregular and infiltrative borders. In the present study, 87.5% cases presented as a mass >5cm and involving fundus, body and isthmus with >1/2 myometrial infiltration.The final diagnosis of LMS is based on the assessment of 3 major histologic features: mitoticactivity, nuclear atypia and tumor cell necrosis proposed by Bell et al[98]. A diffuse moderate to severe nuclear atypia and a coagulative type of necrosis was present in 100% cases. Mitotic count per 10 hpf was > 10 in 7 (77.8%) cases and ≤10 in only 2 cases in our study. However, both these cases had coagulative necrosis along with diffuse moderate to severe nuclear atypia, hence diagnosed as LMS. These findings are in accordance with most studies like Pavithra et al [99] and Giuntoli et al[100] where LMS presented as bulky uterine masses with >1/2 of myometrial infiltration.

LMS is usually identifiable on light microscopy. IHC stains like desmin, smooth-muscle actin and h-caldesmon, may be used to confirm the smooth-muscle origin. All cases subjected to IHC showed positivity for SMA and vimentin with a high Ki-67 index while only 50% cases showed positivity for desmin in the present study.Carvalho et al [101], Nicolas MM et al[102] and Abeler et al[103] showed SMA to be the most sensitive marker for LMS similar to our study. Desmin and h-caldesmon were reported to be less sensitive which is also in agreement with our study.

Endometrial stromal sarcoma

All the cases in the present study infiltrated >1/2 of the myometrium presenting as a mass measuring >5 cm involving the fundus and body in 60% cases of the present study. Microscopy revealed minimal atypia and a low mitotic count (<5/10 HPF) in low grade ESS cases as opposed tohigher mitotic count of >5/10 HPF in high grade ESS. Bhat S et al [104] made similar findings with tumor size ranging from 4-6 cm with low mitotic

count in low grade ESS and a single case showing LVSI. Inthe present study, low grade ESS was consistently positive for CD10, ER and PR. While high grade endometrial stromal sarcomas were consistently positive for cyclin D1 in high grade areas and focal positive for CD10 in low grade areas. This finding is in concordance with Subbaraya et al [105] where CD10 was 100% sensitive and 75% specific, ER and PR were 100% specific and 80% sensitive for low grdae ESS and a diffuse strong cyclin D1 (>70% nuclei) positivity was seen in all 3 cases of high grade ESS. Wang et al [106] also found strong CD10 positivity in 92.86% low grade tumors and cyclinD1 positivity in 87.50% high grade tumors similar to our study. Distinction between low-grade and high-grade tumors is important as the impact on prognosis and therapy is significant.

MALIGNANT MIXED EPITHELIAL AND MESENCHYMAL NEOPLASMS OF UTERINE CORPUS

In our study, all the cases of malignant mixed epithelial and mesenchymal tumors of uterus were of carcinosarcoma/Malignant mixed epithelial and mesenchymal tumor (MMMT). Commonest presenting age group was 61-70 years accounting for 44.44% of the total cases with a mean age of 60.7 years. MMMT was commonly seen in 60 and above age group in a study by AnilaTresa Alukal et al[47].Similarly, Ramondetta et al[107] and RA de Jong et al[108] reported most cases occurring between the sixth and seventh decade with a median age of 62 and 66 years respectively. Carcinosarcomas are bulky tumors. Fifty percent cases in this study involved fundus, body and isthmus with greatest dimension being >5cm in 71.4% and infiltrating >1/2 of the myometrium in 78.6% cases. These findings are in accordance with most published studies on carcinosarcomas like AnilaTresa Alukal et al[47] and Kernochan et al[109] who also observed tumors to be bulkier and larger than endometrial adenocarcinomas. Histology showed a biphasic tumor with malignant-appearing epithelial and mesenchymal elements. In 3 (16.66%) cases,epithelial component was endometrioid carcinoma and in 1 (5.55%)

case the epithelial component was of serous carcinoma.El-Nashar and Mariani[110] reported the epithelial component as papillary serous in 66% and endometrioid 42% cases in his study.Ferguson et al[111] observed one-third of uterine MMMTs with endometrioid differentiation and two-thirds that are serous. However, Meis and Lawrence [112] have reported the endometrioid morphology to be predominant similar to our study.

Out of the total 18 cases of carcinosarcoma, heterologous elements were seen in 7 (38.88%) cases in the present study.Three cases each of rhabdoid and osteoid elements and 4 cases of chondroid elements were reported. Barwick and LiVolsi[113] reported 50% cases presenting with heterologous elements in their study. S. G. Silverberg et al[114] also reported 47.2% cases with heterologus elements.The difference can be attributed tolarger sample size of 34 in Barwick and LiVolsi and 203 in S. G. Silverberg et in comparison to this study. However, the distribution within the heterologous elements in both the studies was similar to ours with most common being rhabdoid followed by chondroid and then osteoid.

Although the diagnosis of carcinosarcoma is a histological one, IHC can be employed to assist. Epithelial component was most commonly positive for CK, ER, PR and CK7 while the mesenchymal component was most commonly positive for vimentin, desmin and SMA in the present study. Myogenin was positive in areas of rhabdoid differentiation. El-Nashar and Mariani[110] made similar findings with positivity of CK in epithelial, vimentin in mesenchymal and myogenin in rhabdoid differentiation. Meis and Lawrence[112] also observed cytokeratin positivity in epithelial component in 100% cases, 81% and 39% cases positive for vimentin and desmin respectively in mesenchymal component. Myogenin was positive in 60% of cases with rhabdoid differentiation.

MALIGNANT NEOPLASMS OF UTERINE CERVIX

There is a wide variation in the incidence of cervical carcinoma across the globe.According to our study the commonest presenting age group was

51-60 years with a mean age of 53.5 years which is similar to Olu-Eddo et al[115] and Zhou et al[116]with a mean age of 50.4 years and 52 years in their respective studies.Misra et al[117] and Kalyani et al[118] also observed that maximum cases presented in women beyond 40 years of age in their respective studies. Bleeding irregularities was the most frequently reported presenting complaint which is similar to the studies done by Mostafa MG et al[119] and Shruthi et al.[120]

Histopathology is a cornerstone in the diagnosis of cervical cancer. In the present study, squamous cell carcinoma predominated in comparison to other histological variants. The spectrum was: 24 (64.86%) cases of non-keratinising squamous cell carcinoma cervix (NKSqCC), 5 (13.51%) cases of endocervical adenocarcinoma (ECC), 4 (10.81%) cases of keratinizing squamous cell carcinoma (KSqCC) and 2 (5.41%) cases of adenosqumaous carcinoma. There was one (2.70%) case each of mucinous carcinoma and small cell neuroendocrine carcinoma of cervix (SCNEC). The distribution of tumours in this study is similar to the study done by Shingleton et al[121] and closely comparable to the studies done by Jeong et al,[122]Alfsen et al[123] and Galic et al[124] where it was observed that in all studies found that squamous cell carcinoma cervix was the most common cervical neoplasm.

Squamous cell carcinoma

Amongst SqCC, NKSqCC was more common compared to KSqCC accounting for 66.67% and 10.81% cases respectively. NKSqCC was composed of polygonal squamous cells arranged in sheets and nests with absence of keratin pearls while all cases of KSqCC showed keratin pearls.S. Shrikanth[125] also reported higher incidence of NKSqCC compared to SqCC accounting 26.6% and 12.3% respectively with similar hitological findings in his study. A diffuse strong positivity for p16 and p40 was seen in 100% cases with available IHC in the present study.Stoler MH et al[126] also found that P16 expression was diffuse in 100% of invasive cancers. P16 expression showed block positivity in 89.3% cases

in Kalyani et al[118] study. In a study by Sarwath H et al[127] block positivity was seen in 92.2% of cases with sensitivity of 79.2%. Similarly, Amaro-Filho[128] has reported P16 expression as diffusein 85.5% of SCC of cervix in his study. P16 has emerged as a surrogate marker for in-situ as well as advanced cervical cancer.

Endocervical adenocarcinoma, usual type

The incidence of ECC, the second most common cervical cancer in the world, has been on the rise. There were 5 (13.89%) cases all of which were of usual type. Similarly, ECC accounted for 14% of cervical carcinomas according to a study done by Dikshit et al.[129] Diffuse strong positivity for p16 with a negative WT1 and p53 was seen in all cases.ER was negative in 2 cases but focal positive in 1 case. These findings are comparable to Stolnicu et al[130] who reported 90%, 5% and 3.6% positivity for p16, ER and p53 respectively of the total cases examined in his study.

Adenosquamous carcinoma

Diagnosis of adenosquamous carcinoma of cervix might be difficult and a histology-driven approach is emerging as a clinical strategy, identifying high-risk patients. There were 2 cases in the present study accounting for 5.41% of total malignant neoplasms of uterine cervix. Both malignant glandular and squamous differentiation was present on histology. Yordonav et al[131] and Zhou et al[116] recorded the incidence of adenosqumaous carcinoma cervix as 3.2% and 3.4% of all cervical neoplasm in their respective studies. The difference may be explainedby a longer study period of 10 years inYordonav et al study compared to 5 years in this study and a larger sample size of 8751 in Zhou et al study compared to 37 in ours.Regardless of the small number of patients, adenosquamous carcinoma has a worse prognosis than squamous cell carcinoma.

Mucinous Carcinoma

There was a solitary case of mucinous carcinoma of intestinal type in our study which presented as cervical mass reaching upto the isthmus.

Histology revealed tumor cells arranged in glandular configuration and showed goblet cells along with extracellular pools of mucin. Mucinous adenocarcinoma of the uterine cervix is a rare subtype of cervical cancer with intestinal type being even rarer as observed by Bonin et al[132] with only six (29%) out of the 21 cases of mucinous adenocarcinoma cervix in his study being intestinal type all of which had the characteristic feature of presence of goblet cells as in our case. K Mardi[133] and Shintaku et al[134] also made similar histomorphological findings in their respective case studies.

Small cell neuroendocrine carcinoma cervix

These are rare highly aggressive tumors of the cervix.There was a solitary case in our study presenting with a growth confined to the cervix. Tumor cells were arranged in sheetshaving a small round hyperchromatic nucleus with scanty cytoplasm and nuclear moulding. LVSI, brisk mitosis and involvement of bilateral parametrium was noted. CK showed a dot like positivity, chromogranin was focal positive, CD56 and NSE were weak positive and synaptophysin was negative in our case. Viswanathan et al[135] reported similar findings with only 11 of the 21 SCNEC tumors of cervix included in his study staining positive for all three markers i.e chromogranin, synaptophysin or CD56. Pavithra et al[136] also reported similar findingsin her case report wherethe tumour cells showed positivity for cytokeratin and synaptophysin. However, chromogranin was negative. Correlating immunohistochemical findings with the histopathological appearance led to the diagnosis of SCNEC of the cervix similar to our case.

So, as the female genital tract malignancies form a huge burden of morbidity and mortality in India, there is a need to establish better screening programmes aimed at early detection and also to educate regarding early symptoms of the disease. It was observed by integrating morphology with immunohistochemistry, definitive diagnostic information can be provided.

SUMMARY AND CONCLUSION

Malignant tumors of the female reproductive system are an important cause of morbidity and mortality worldwide. Histopathological examination is the key component to diagnose and rule out malignancy and is compulsory for all the surgical specimens.

In this study we analysed the histomorphological characteristics of 239 malignant uterine neoplasms and correlated them with immunohistochemistry wherever possible and the findings are –

1. A total of 71,656 histopathology specimens were received during this study period, out of which, 6976 were hysterectomies, endometrial curettes/biopsies and cervical punch and cone biopsies. Out of these, 239 (3.42%) were malignant uterine tumors.
2. Hysterectomy was the commonest surgical specimen received accounting for 77.82% cases.
3. Of the total 239 cases, 202 (84.87%) originated in the uterine corpus and 37 (15.48%) were of the uterine cervix.
4. Overall maximum females affected by uterine malignancies were within the age group of 51-60 years with a mean age of presentation being 58.2 years.
5. Post-menopausal bleeding was the most common clinical presentation seen in 144 (60.25%) of the total 239 cases.
6. Malignant neoplasms of epithelial origin predominated amongst all the neoplasms of uterine corpus accounting for 82.18% of the cases with 51-60 years being the commonest age group of presentation.
6. Endometrioid carcinoma was the commonest epithelial malignancy of uterine corpus accounting for 150 (90.36%) cases out of which, 66% cases were categorized as FIGO grade I.
7. Some rare malignancies like endometrial de-differentiated carcinoma (1.20%) and solitary case of endometrial clear cell carcinoma were encountered.

8. A mass involving fundus, body and isthmus of uterus was the most common, accounting for 47.6% and 60% cases of endometrioid and serous carcinoma of uterus respectively.
9. More than half of myometrial invasion was more common in serous carcinoma (66.67%) in comparison to endometrioid carcinoma (43.5%).
10. Serous carcinomas arose more commonly in a background of senile cystic atrophy (61.53%) of the endometrium, while endometrioid carcinoma was more commonly seen in the background of atypical endometrial hyperplasia (9.33%).
11. Majority of the cases of endometrioid carcinomas showed a diffuse strong positivity for ER and PR with wild type positivity for p53 and a negative WT1. Ki-67 index ranged between 15-90% which varied according to tumor grade.
12. Serous carcinomas showed a diffuse strong positivity for p53 and a high Ki-67 index in all caseswith available IHC.
13. Commonest age group of presentation was 31-40 years for malignant mesenchymal neoplasms of uterine corpus.
14. Leiomyosarcoma was the commonest malignant mesenchymal tumors seen in 9 (50%) cases and was found to be positive for SMA and vimentin with a high Ki-67 index on IHC.
15. Maximum cases of leiomyosarcoma (87.5%) involved fundus, body and isthmus of uterus. While 80% cases of ESS involved fundus and body alone.
16. LGESS were most commonly positive for CD10 along with ER and PR with a low ki-67 index. While HGESS were consistently positive for cyclin D1.
17. All the 18 cases of malignant mixed epithelial and mesenchymal neoplasms of uterine corpus were of carcinosarcoma with 61-70 years being the commonest age group.

18. Eleven (78.6%) cases of carcinosarcoma infiltrated >1/2 of the myometrium with 50% cases involving the fundus, body and isthmus of uterus.
19. Heterologous elements were seen in 7(38.88%) cases, out of which 3 cases had osteoid and 4 cases had chondroid elements respectively.
20. Commonest presenting age group for malignant uterine cervix neoplasms was 51-60 years with a mean age of 53.5 years.
21. Non- keratinising squamous cell carcinoma was the commonest histological subtype accounting for 64.86% cases followed by 13.51% cases of endocervical adenocarcinoma and 5.41% cases of adenosquamous carcinoma.
22. A diffuse strong p16 with a negative ERand WT1 was seen in majority of the cases of endocervical adenocarcinoma with available IHC.
23. Solitary cases of rare malignancies involving the cervix which includedmucinous carcinoma of intestinal type and small cell neuroendocrine carcinoma each were also seen.

To conclude, uterine neoplasms are a heterogeneous group of tumors and are diagnostically challenging. Correlation of histomorphological findings with immunohistochemistry (wherever possible) is important to give a definitive diagnosis as the management varies for different histological subtypes.

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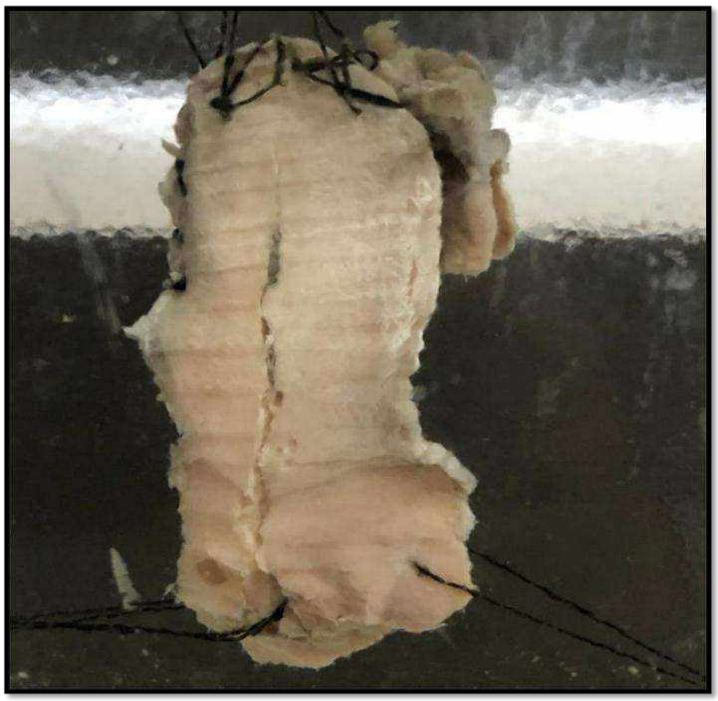
Picture 1:-Endometrial Endometrioid carcinoma (gross a)-tan to white growths involving the fundus, body an isthmus of uterus and infiltrating less than half of myometrium

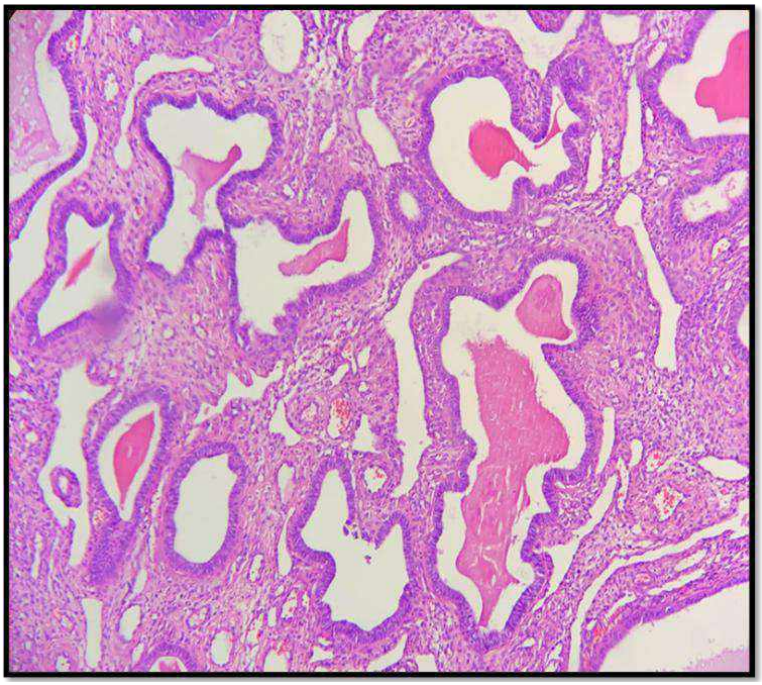
Picture 2:- Endometrial Endometrioid carcinoma (gross b)- tan to white ulceroproliferative growth involving fundus, body and isthmus of uterus and infiltrating more than half of the myometrium

Picture 3:-Uterine Leiomyosarcoma (gross)- tan to white infiltrative mass filling the entire uterine cavity and reaching up to isthmus.

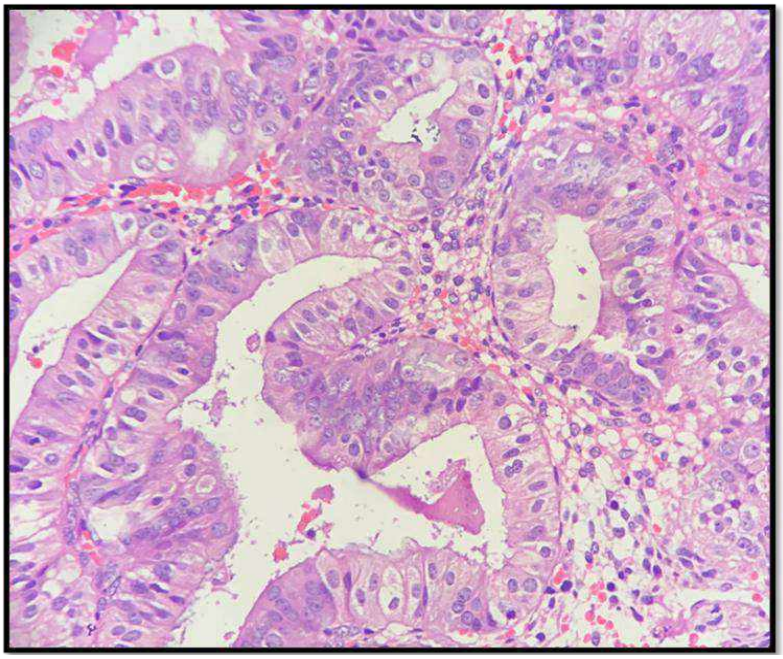
Picture 4:-Non- Keratinizing Squamous Cell Carcinoma Cervix (gross)- mounted specimen showing an exophytic growth involving both the lips of cervix and extending upto isthmus.



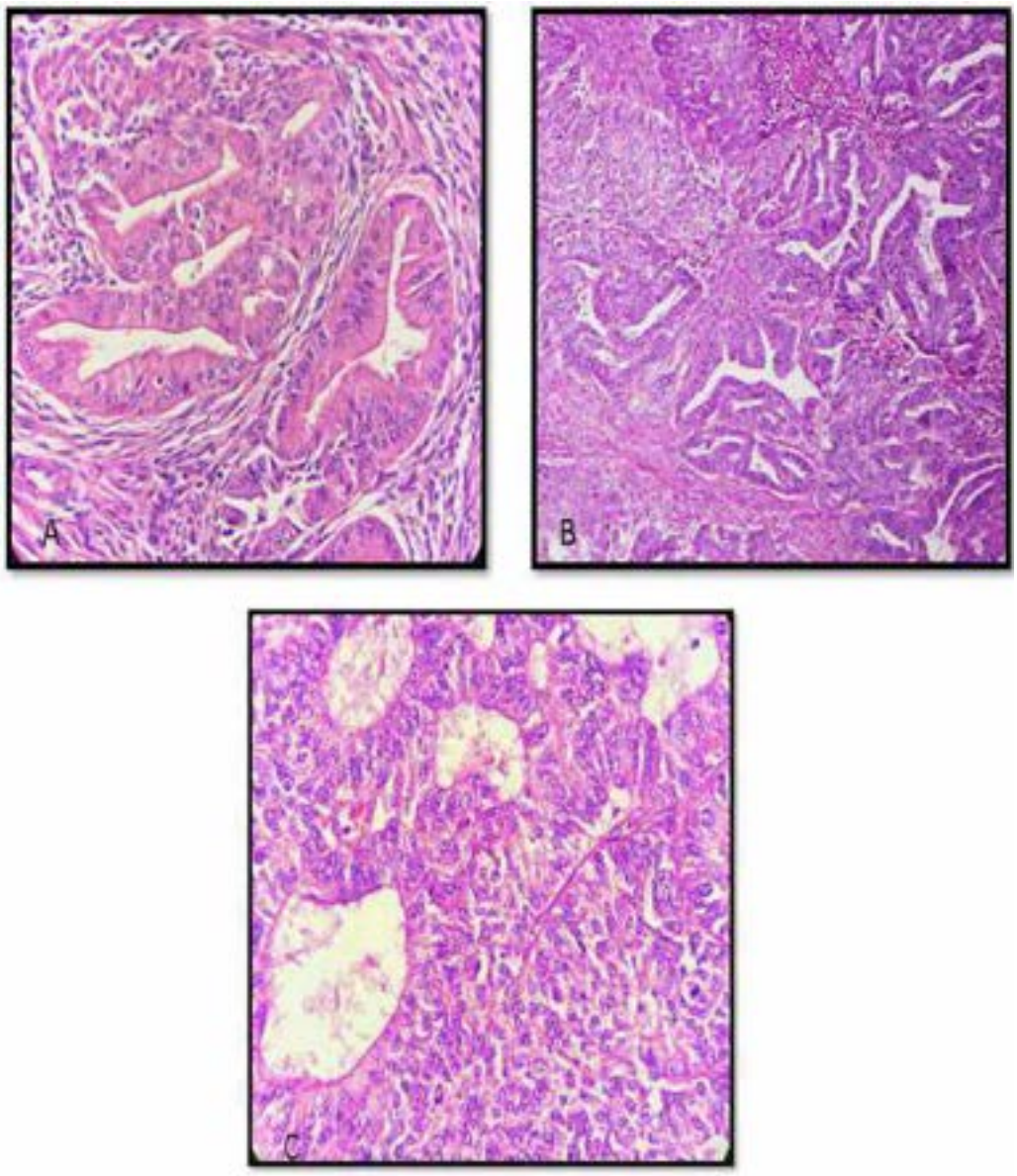
Picture 5:-Small Cell Neuroendocrine Carcinoma Cervix (gross)- gross image of mounted specimen showing an endophytic mass involving both the lips of cervix.



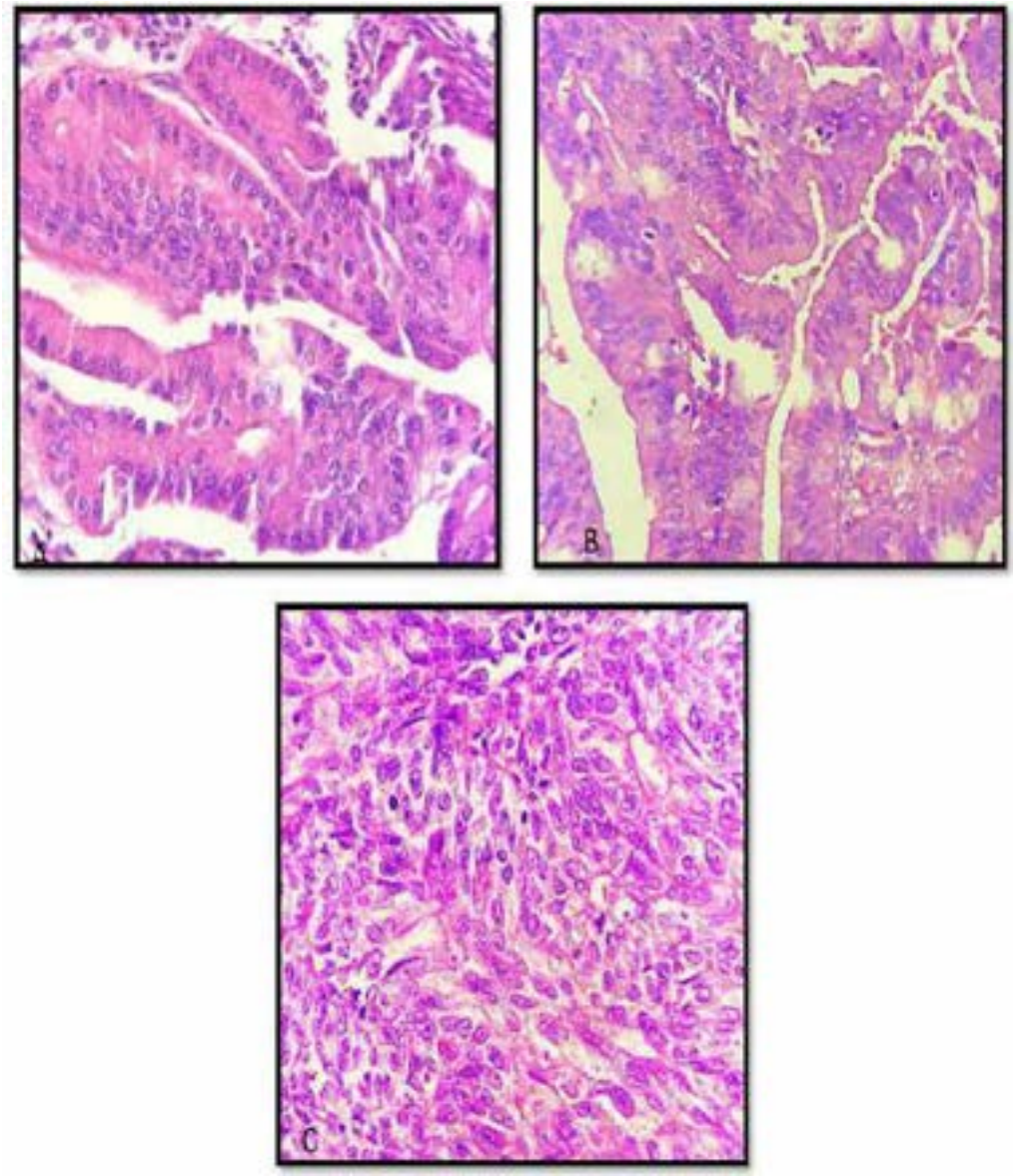
Picture 6:- Endometrial hyperplasia without atypia- minimaly to mildly crowded cystically dilated endometrial glands with focal out pouching, devoid of nuclear atypia (H&E,100X)



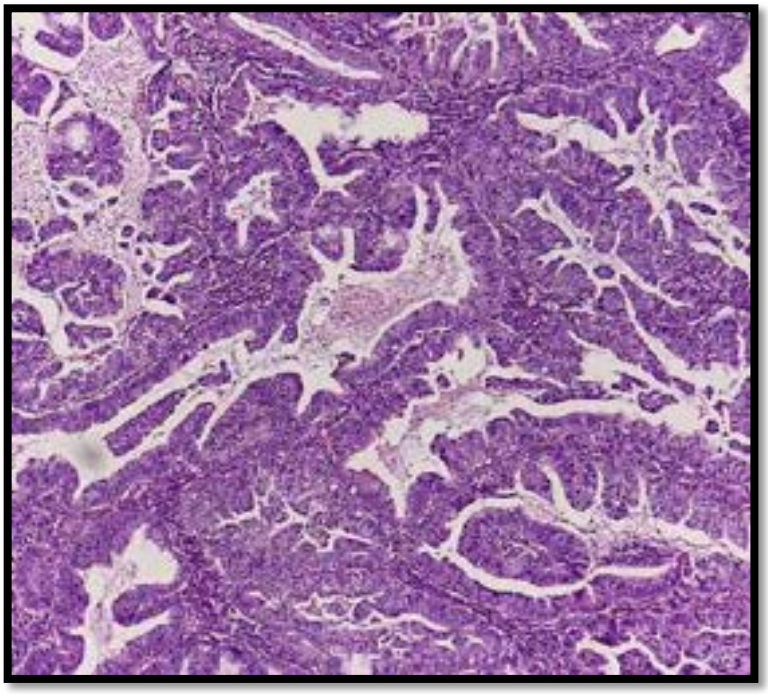
Picture 7:- Atypical hyperplasia endometrium- closely packed atypical endometrial glands with little intervening stroma, having nuclear stratification and loss of polarity. (H&E, 400X)



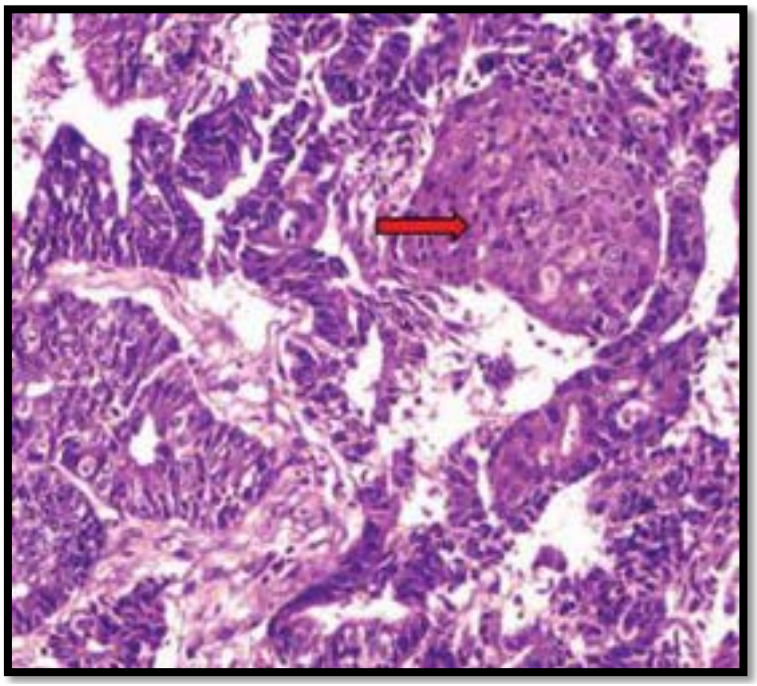
Picture 8:- Endometrial Endometrioid carcinoma: Architechural grading: FIGO grade I (A), FIGO grade II(B), FIGO grade III(C) (H&E, 100X)



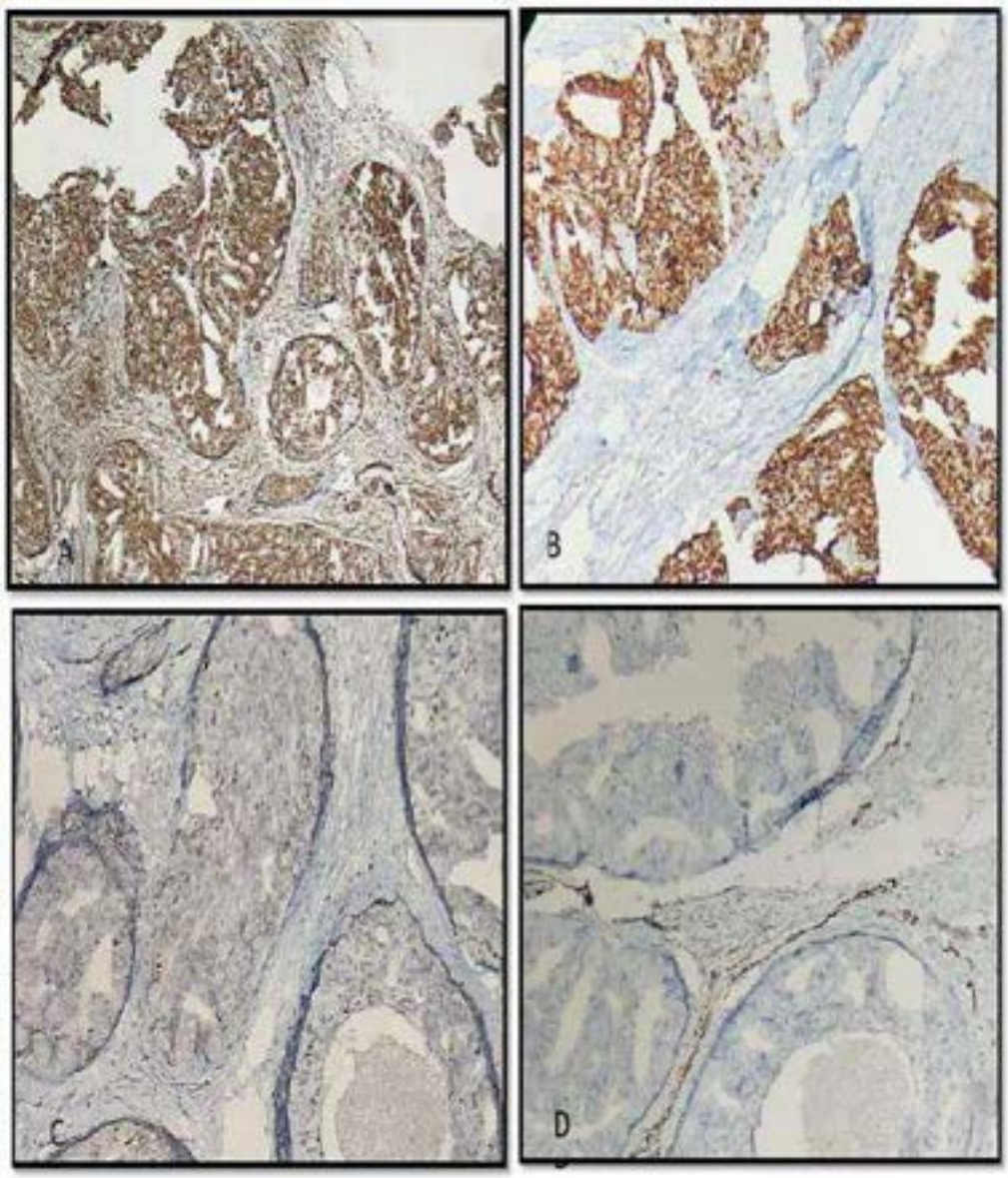
Picture 9:- Endometrial Endometrioid carcinoma: Nuclear grading: FIGO grade I(A), FIGO grade II(B), FIGO grade III(C) (H&E,400X)



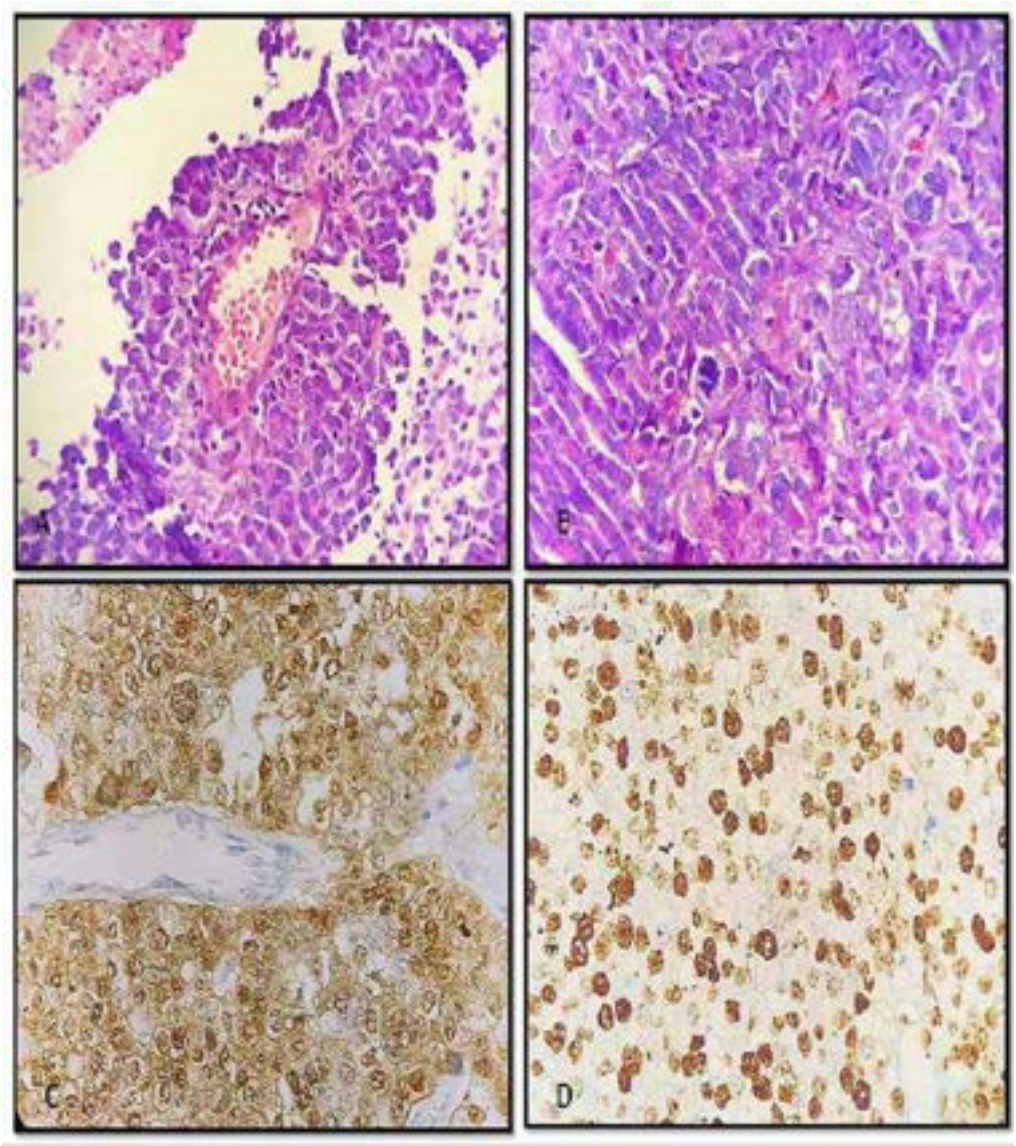
Picture 10:- Endometrial Endometrioid carcinoma FIGO grade I with a predominant Villoglandular arrangement (H&E, 100X)



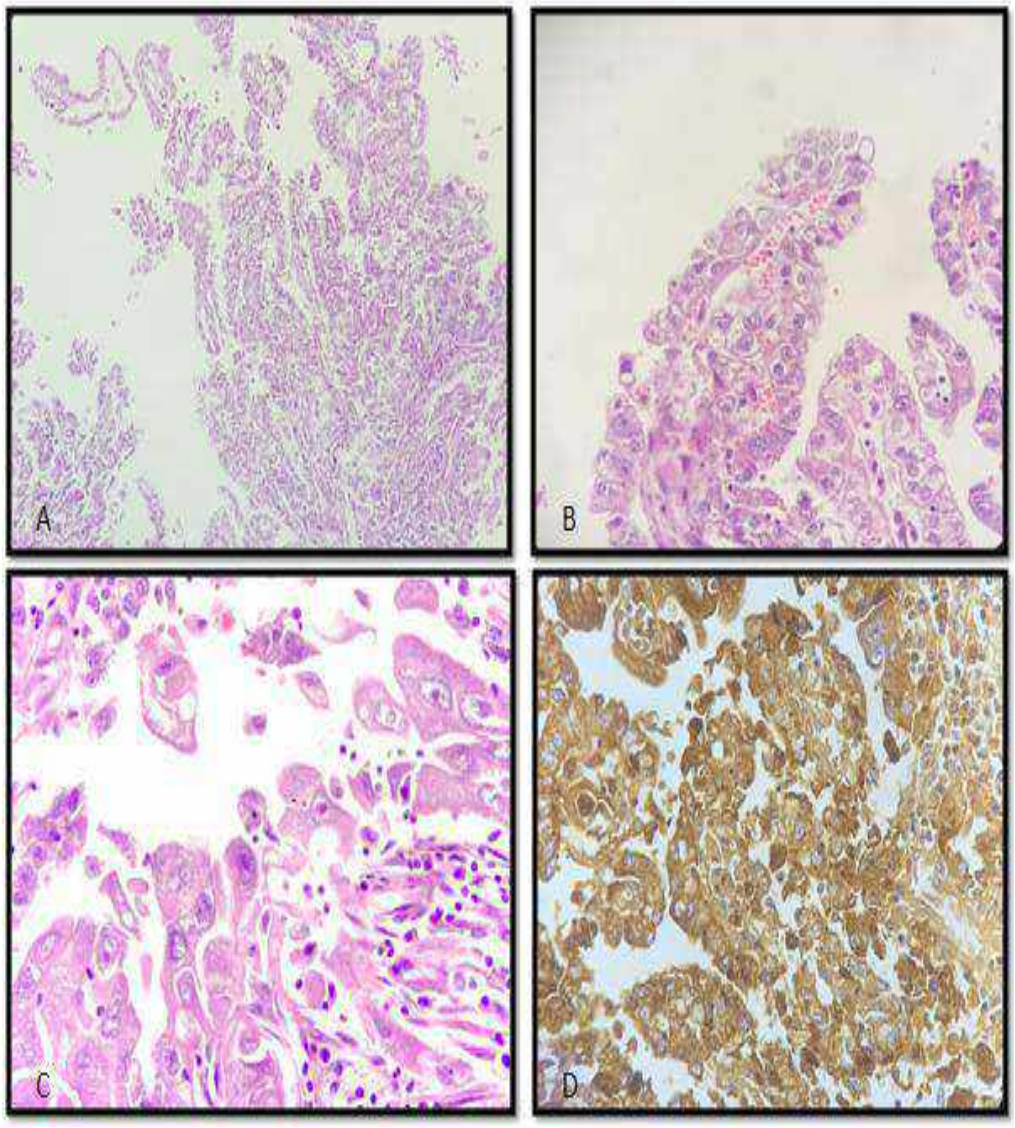
Picture 11:- Endometrial Endometrioid carcinoma FIGO grade II showing squamous morules (red arrow) surrounded by glandular component (H&E,400X)



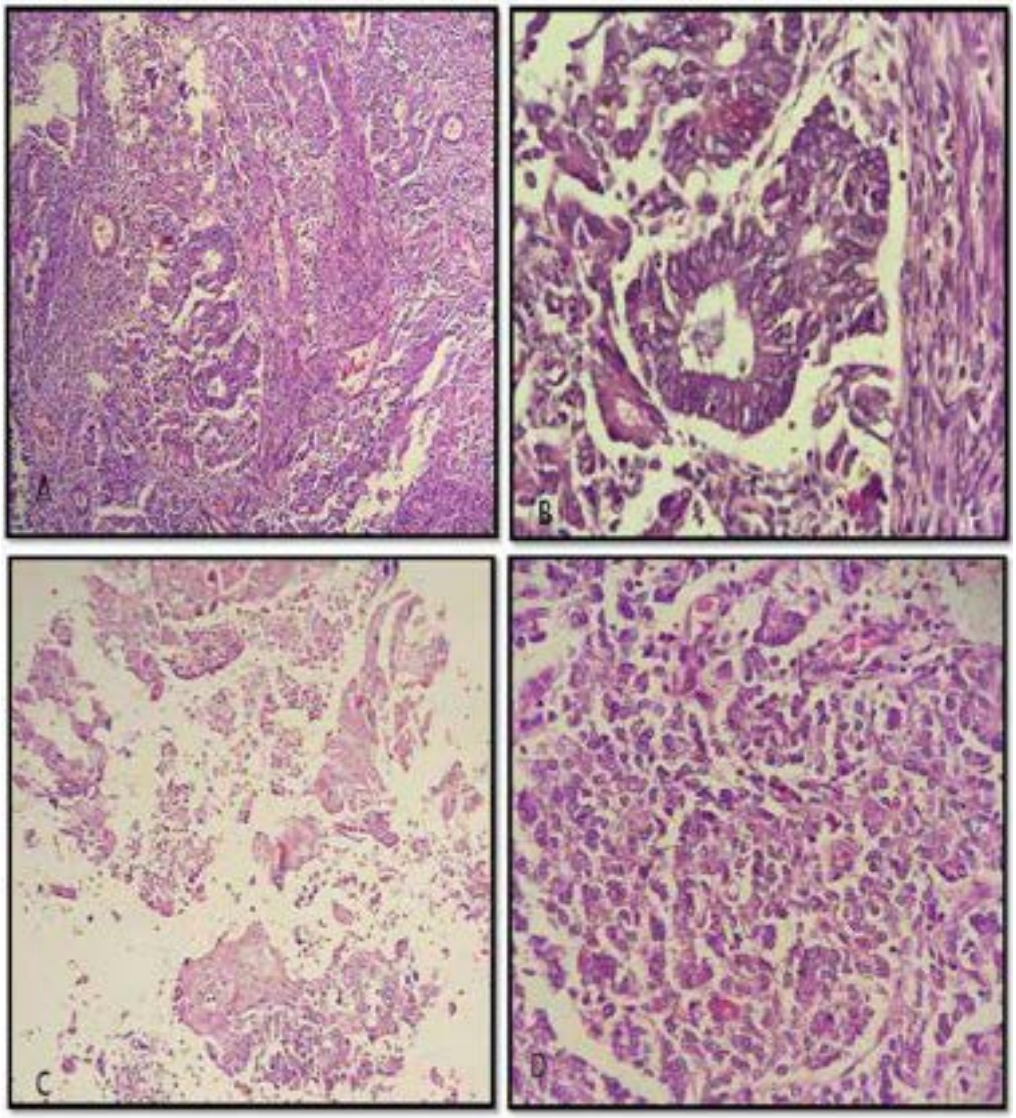
Picture 12:- Endometrial Endometrioid carcinoma- diffuse strong nuclear immunopositivity of ER and PR (A and B respectively)(100X), wild type immunopositivity of p53 (C,100X), immunonegativity of WT1 (D,100X)



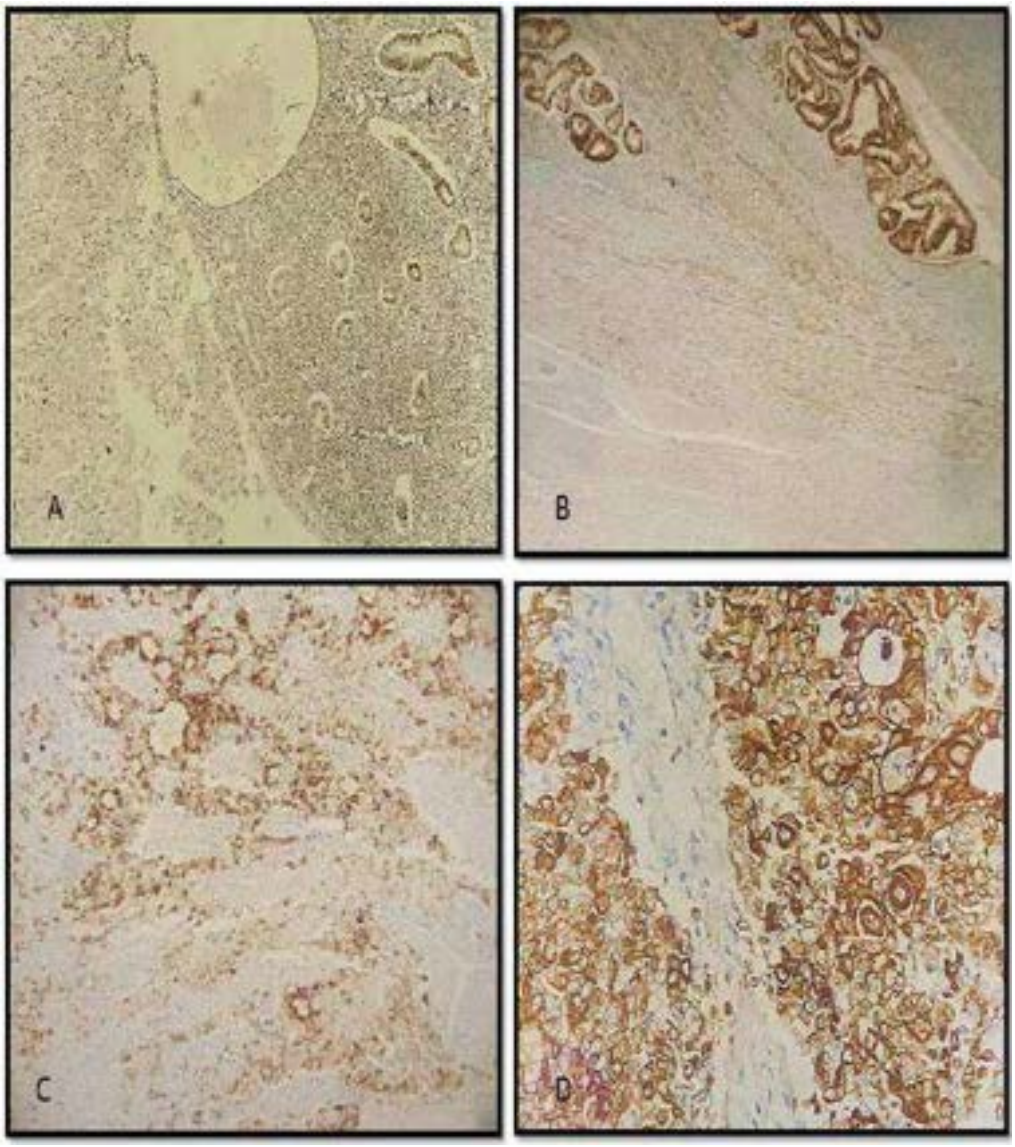
Picture 13:- Serous carcinoma endometrium- showing complex glandular and papillary pattern (A) (H&E,100X), showing nuclear pleomorphism with prominent nucleoli and mitosis (B) (H&E,400X), diffuse strong nuclear immunopositivity of p53 (C)(400X), Ki-67 proliferation index >50% (D) (400X)



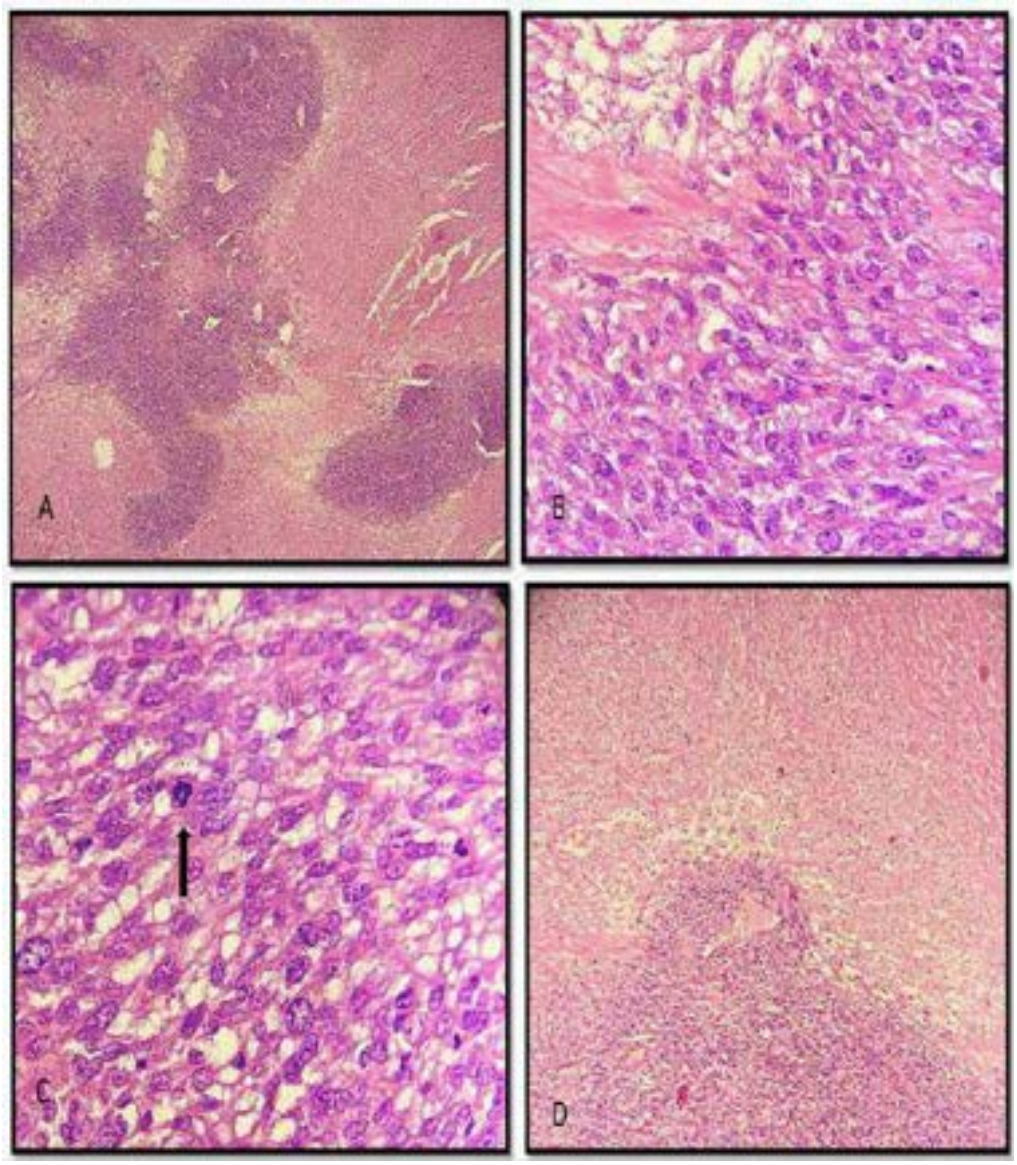
Picture 14:- Clear cell carcinoma endometrium- showing predominant papillary and focal glandular pattern (A)(H&E,100X), having hobnail shaped cells with moderate eosinophilic cytoplasm and clearing at places (B and C)(H&E400X), diffuse strong cytoplasmic immunopositivity of Napsin A (D)(400X)



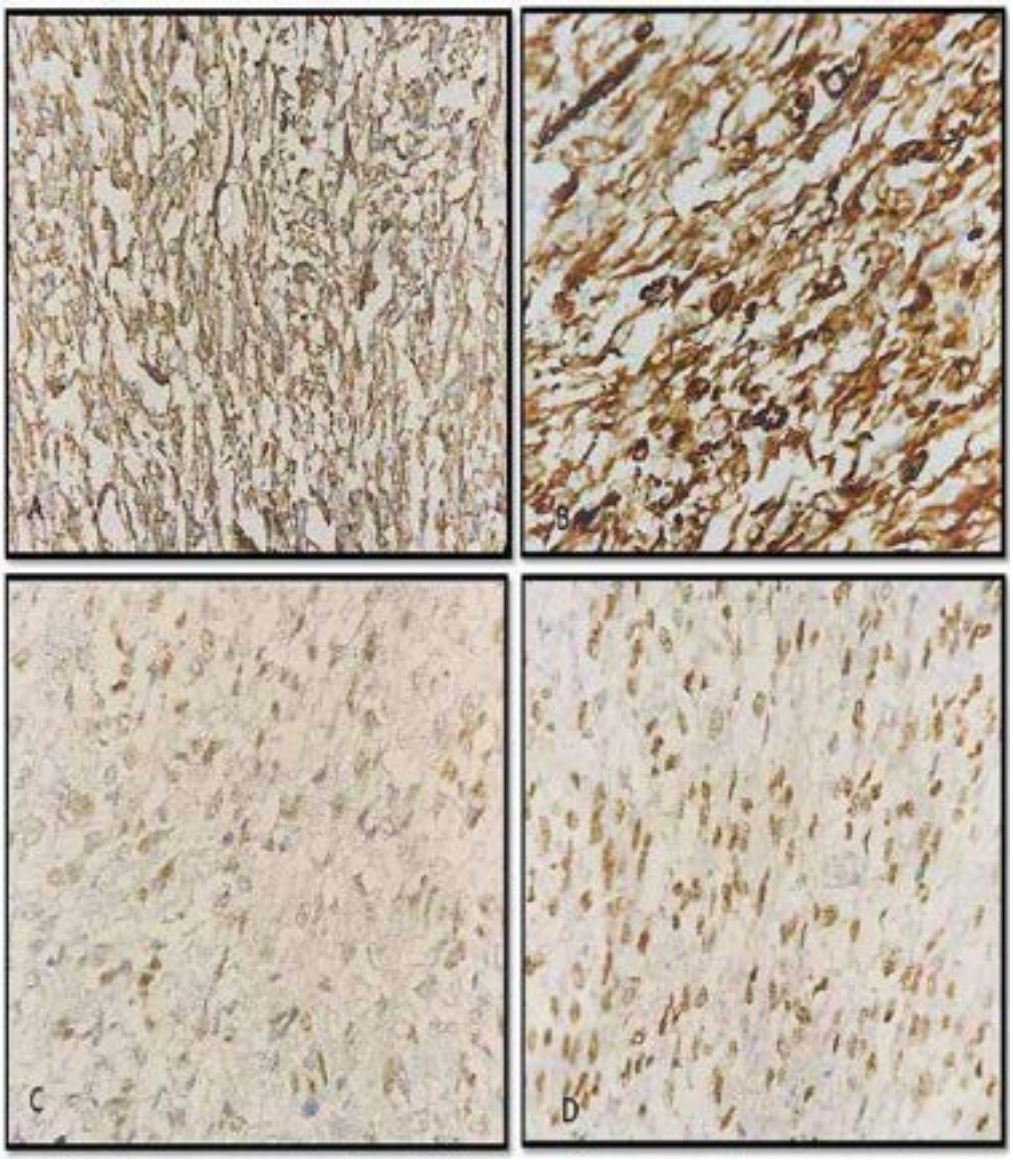
Picture 15:- De-differentiated carcinoma endometrium- showing both undifferentiated and well-differentiated components (A)(H&E,100X), well differentiated component showing morphology of endometrioid carcinoma FIGO grade II (B) (H&E,400X), foci of squamous differentiation (C)(H&E,400X), undifferentiated component (D)(H&E,400X)



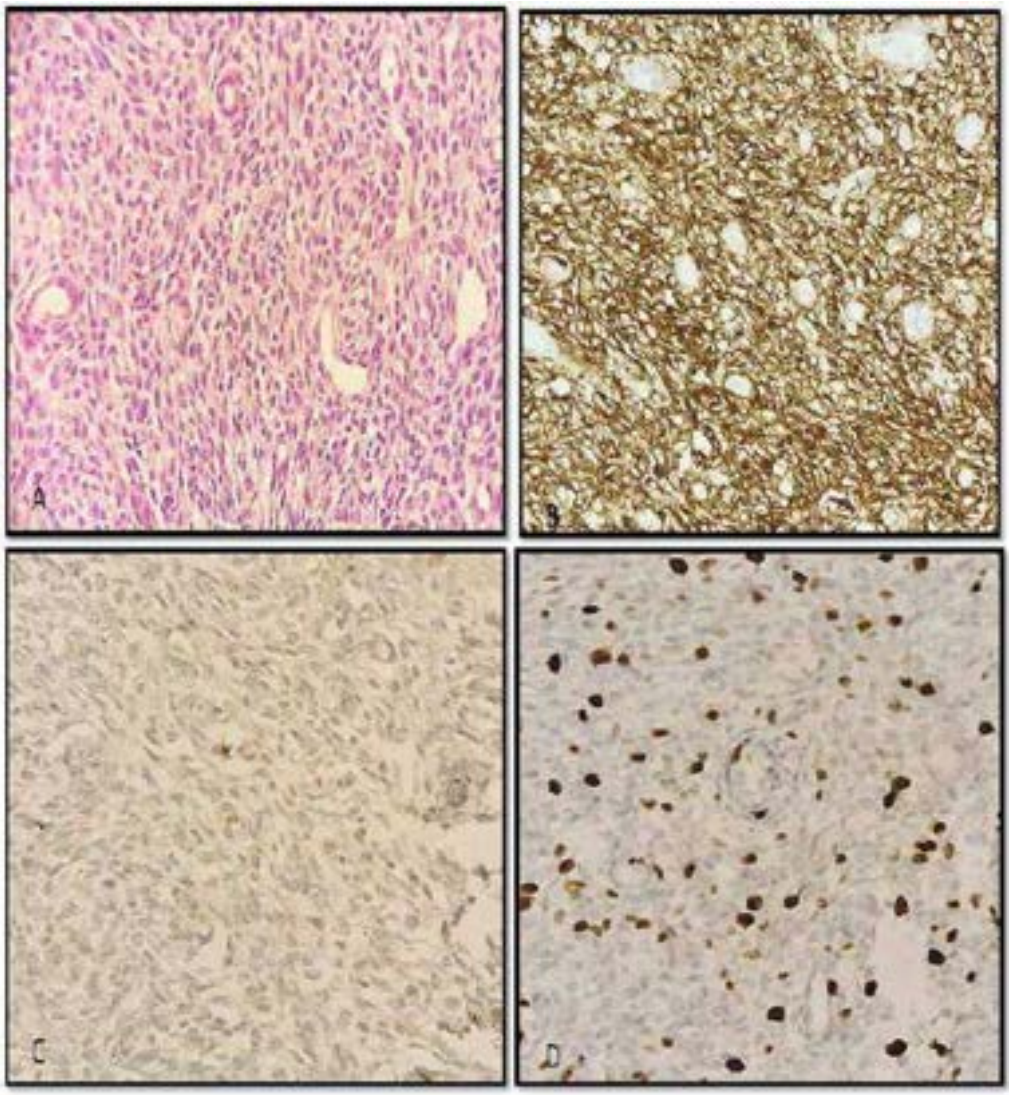
Picture 16:- De- differentiated carcinoma endometrium- showing immunopositivity of ER and PR in well differentiated component (A and B respectively)(100X); immunopositivity of EMA and CK8/18 in undifferentiated component (C and D respectively, 100X)



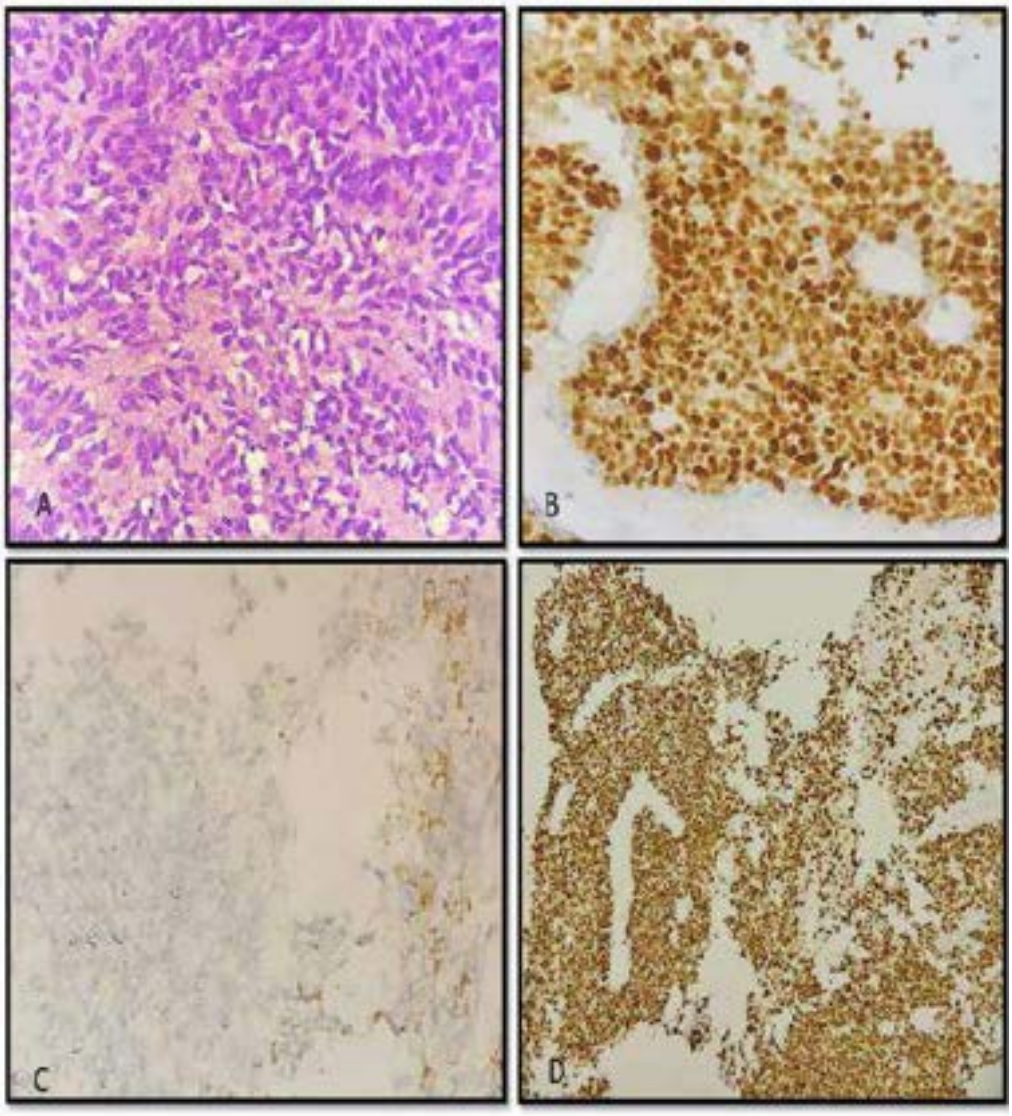
Picture 17:- Uterine Leiomyosarcoma- showing intersecting fascicles composed of highly atypical spindled cells(A) (H&E,100x), diffuse nuclear atypia having hyperchromatic nuclei with prominent nucleoli (B) (H&E,400X), brisk mitosis with atypical mitotic figures (C)(H&E,400X), coagulative type of tumor cell necrosis (D)(H&E,400X)



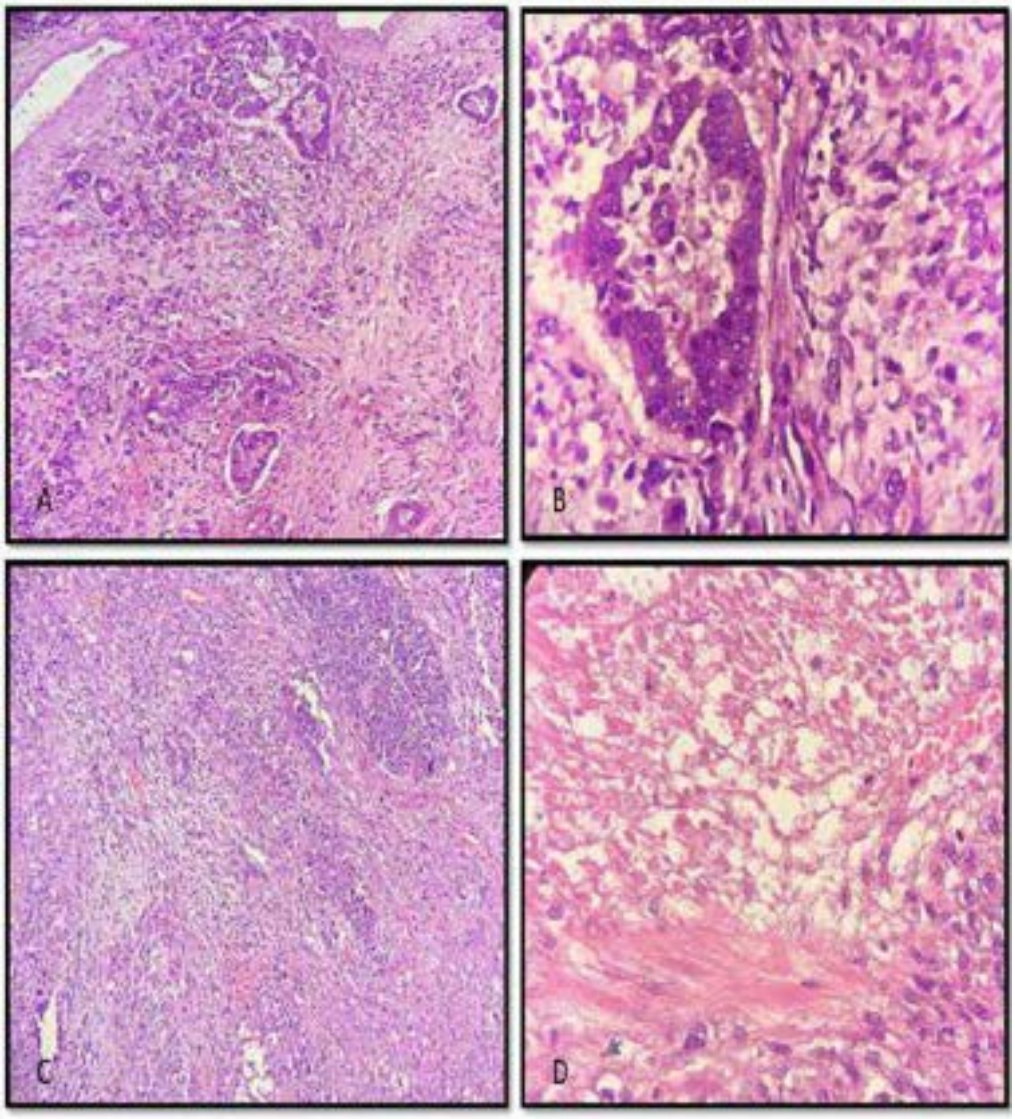
Picture 18:- Uterine Leiomyosarcoma- showing diffuse strong membranous immunopositivity of SMA (A)(H&E,400X), diffuse strong cytoplasmic immunopositivity of vimentin (B) (H&E,400X), focal nuclear immunopositivity of ER (C)(H&E,400X), Ki-67 proliferating index of >50% (D)(H&E,400X)



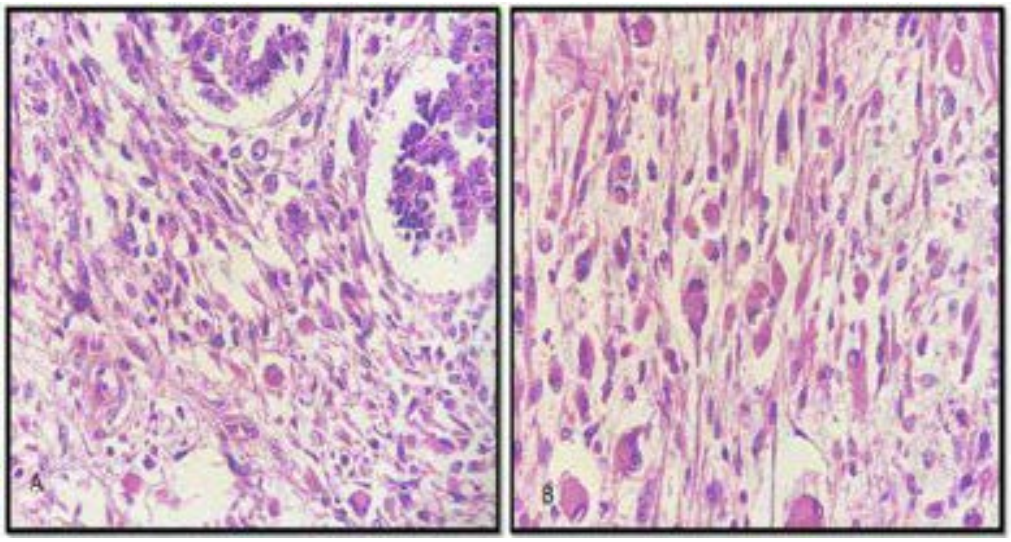
Picture 19:- Low- Grade Endometrial Stromal Sarcoma- showing sheets of tumor cells with interspersed arteriole type small vessels, minimal atypia and no mitosis (A)(H&E,400X), diffuse strong cytoplasmic immunopositivity of CD10 (B)(100x), immunonegativity of cyclin D1 (C)(100X), Ki-67 proliferation index <50% (D)(100X)



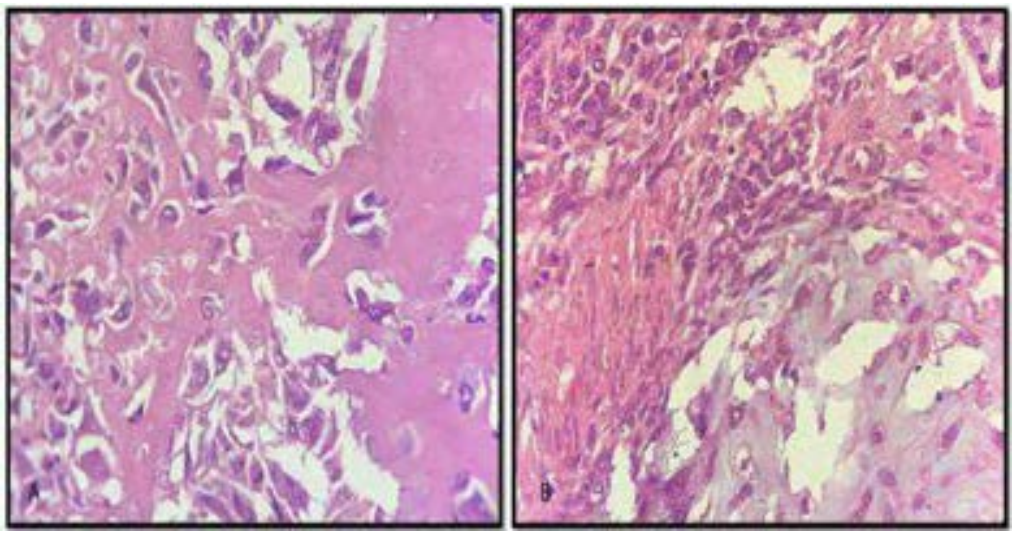
Picture 20:- High- Grade Endometrial Stromal Sarcoma- round to oval cells having ill-defined cytoplasm, nuclear atypia and mitosis (A)(H&E,400X), diffuse strong nuclear immunopositivity of cyclin D1 in high grade areas (B)(400X), focal weak immunopositivity of CD10 in low grade areas (C)(100X), Ki-67 prolifertaion index >90% (D)(100X)



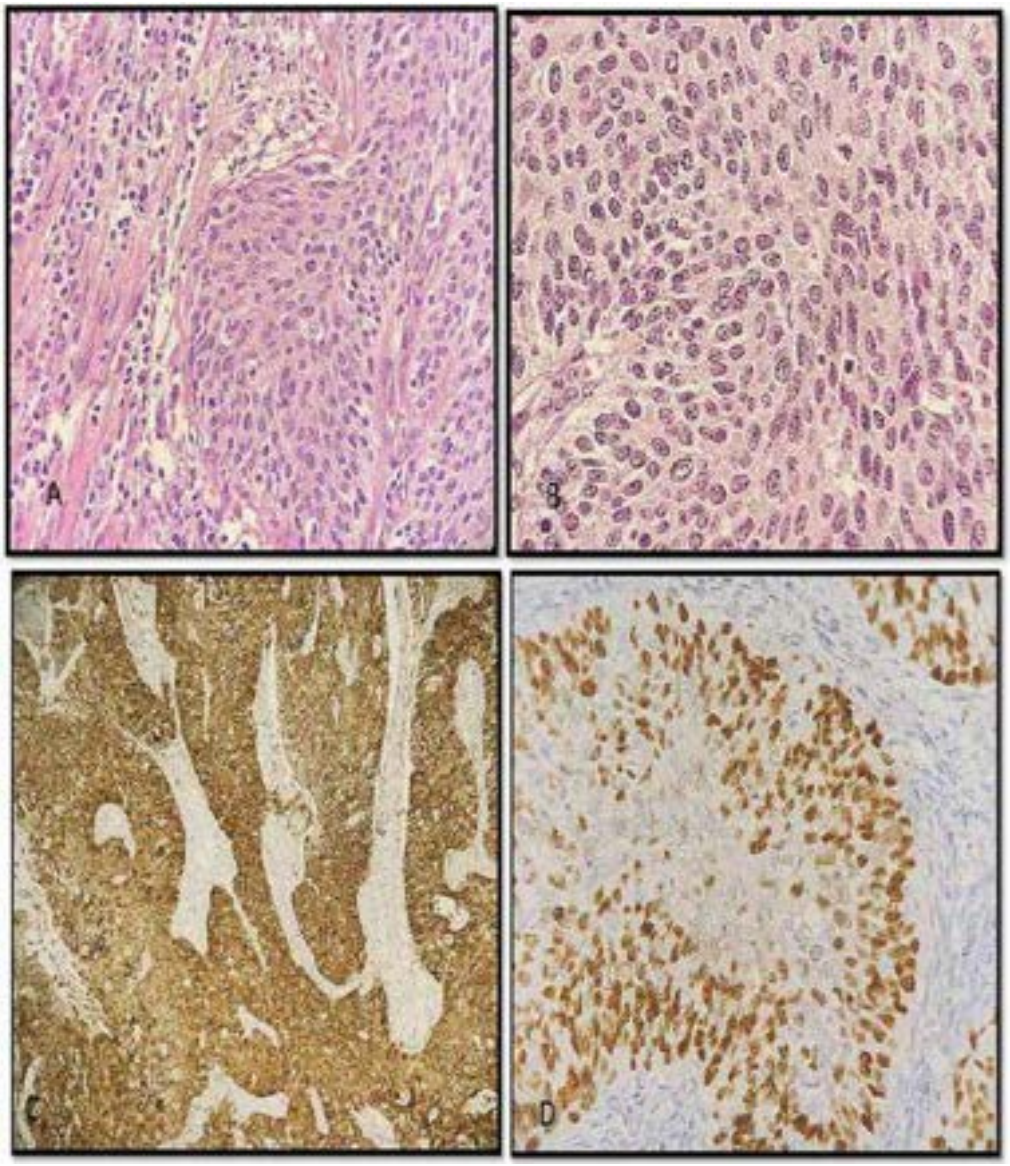
Picture 21:- Uterine Carcinosarcoma/MMMT- biphasic tumour composed of malignant epithelial and mesenchymal component (A)(H&E,100X), epithelial component seen as endometrioid carcinoma (B)(400X), mesenchymal component seen as pleomorphic spindle cells (C)(400X), areas of necrosis(D)(400X)



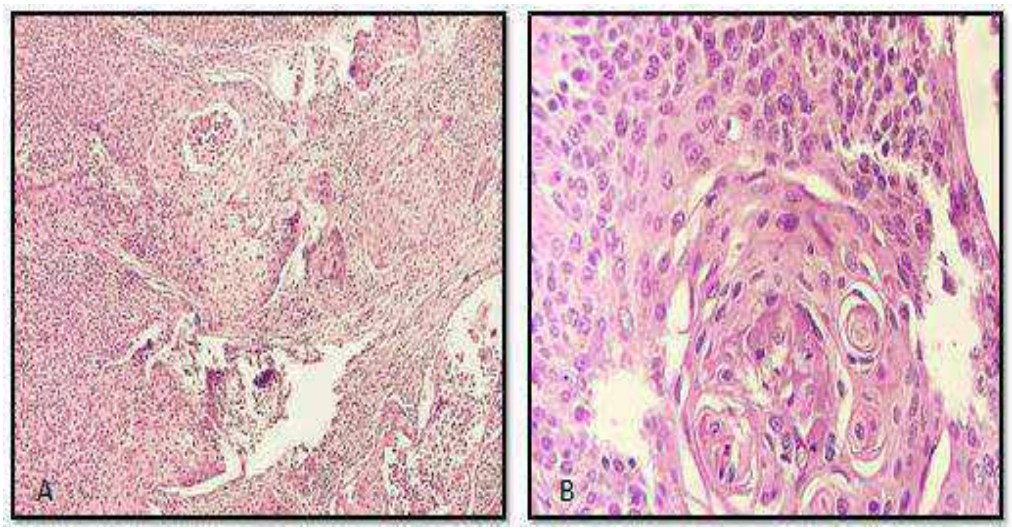
Picture 22:- Uterine Carcinosarcoma/MMMT- sarcomatous component showing rhabdoid differentiation (A) (H&E, 100X), pleomorphic large cells with abundant eosinophilic cytoplasm (B)(H&E,400X)



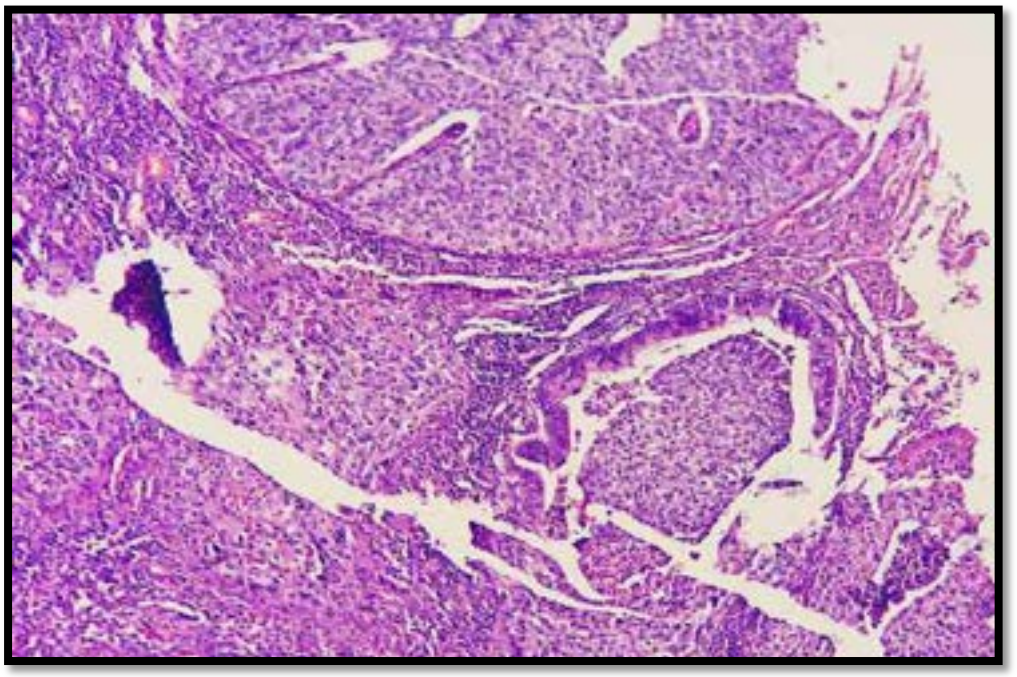
Picture 23:- Uterine Carcinosarcoma/MMMT-heterologous sarcomatous elements seen as osteoid (A)(H&E,400X) and chondroid(B)(H&E,400X)



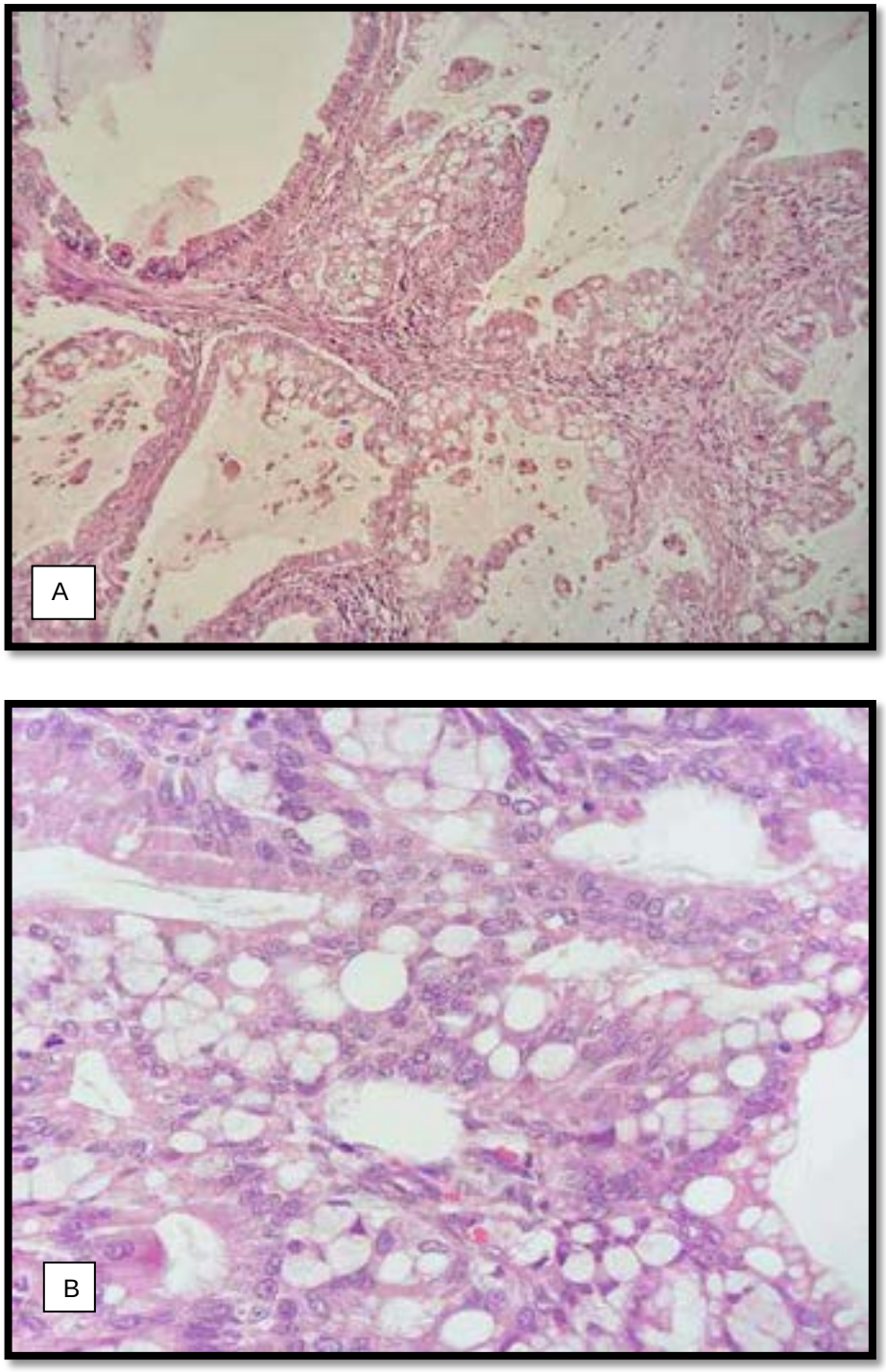
Picture 24:- Non-Keratinising squamous cell carcinoma cervix- polygonal squamous cells arranged in sheets and nests. (A)(H&E,100X), cells have a large round nucleus with a conspicous nucleoli and moderate to abundant cytoplasm. No keratin pearls seen (B)(H&E,400X),diffuse strong cytoplasmic and nuclear immunopositivity of p40 (C)(100X), diffuse strong nuclear immunopositivity of p16 (D)(400X)



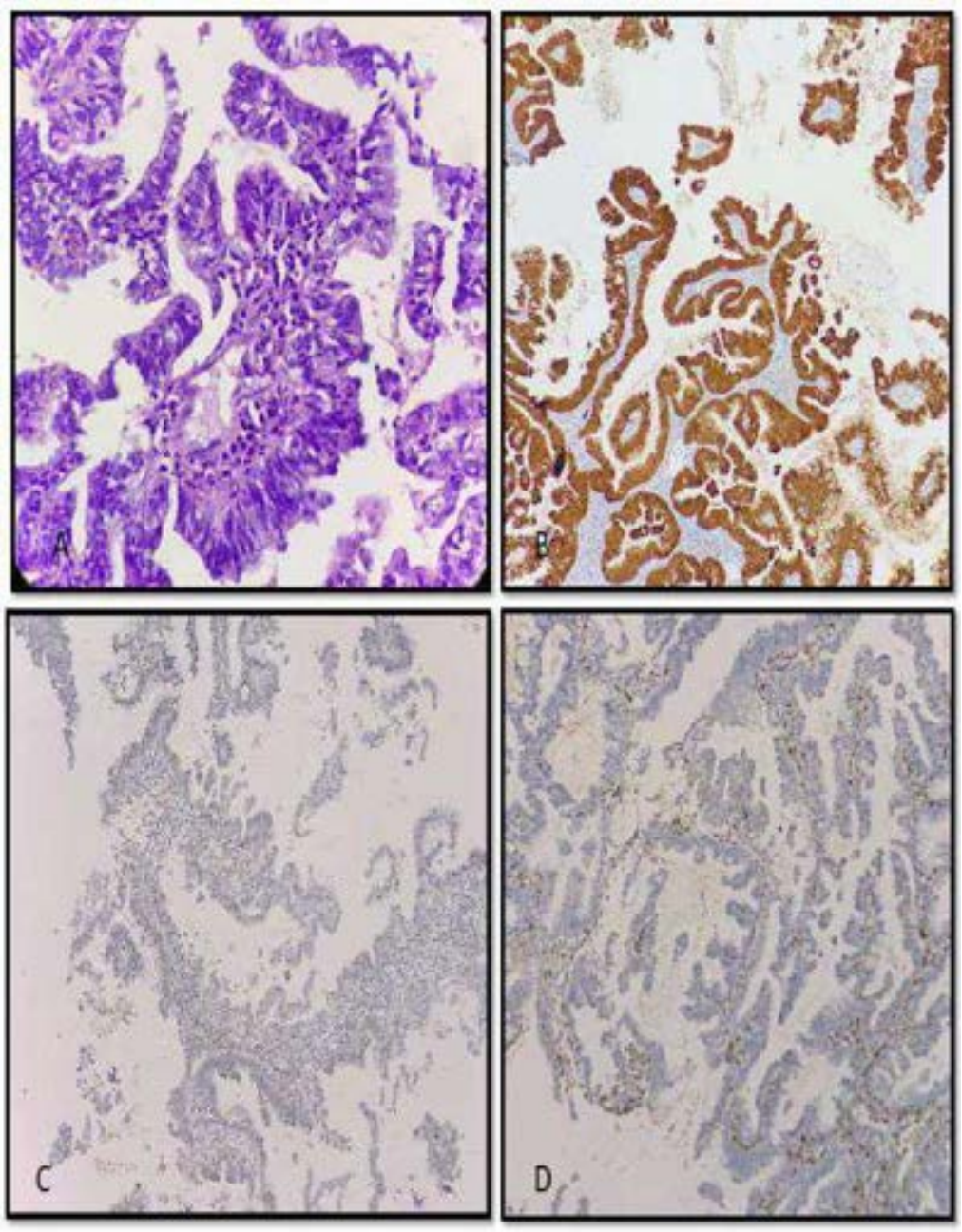
Picture 25:- Keratinising squamous cell carcinoma cervix- polygonal squamous cells arranged in nests(A)(H&E,100X), keratin pearls (B)(H&E,400X)



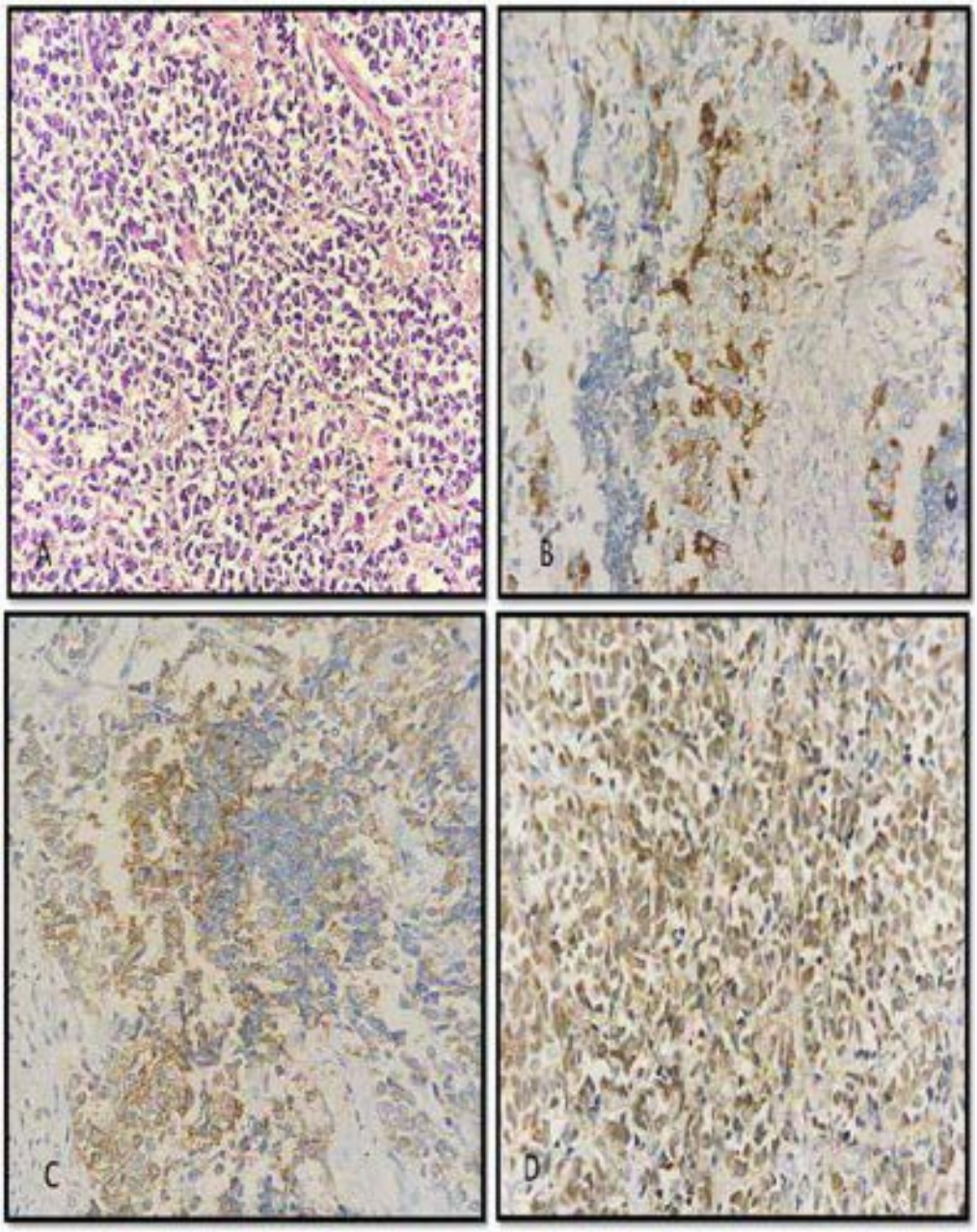
Picture 26:- Adenosquamous carcinoma cervix- Tumor cells arranged in nests and sheets along with areas having presence of glands lined by cells exhibiting nuclear hyperchromasia and stratification (H&E,100X)



Picture 27:- Mucinous carcinoma cervix, intestinal type- glandular configuration with extracellular pools of mucin (A,H&E,100X) prominent goblet cells (B,H&E,400X)



Picture 28:- Endocervical adenocarcinoma, usual type- (A)(H&E,100X), diffuse strong block like immunopositivity of p16(B)(H&E,100X), immunonegativity of p53(C)(100X), immunonegativity of ER in tumor cells(D)(100X)



Picture 29:- Small cell neuroendocrine carcinoma cervix- sheeting pattern with nuclear moulding(A)(H&E,400X), focal strong cytoplasmic immunopositivity of chromogranin (B)(H&E,400X), focal weak membranous immunopositivity of CD56(C)(400X), focal weak cytoplasmic immunopositivity of NSE (D)(400X)

PROFORMA

Sr. No. _____

Name Age Sex

MRD No. Date

Histopath No. Address

Brief history:

Investigations (Any radiological/ biochemical findings):

Type of specimen:

Gross examination:

Microscopic examination:

IHC (if done):

Final histopathological diagnosis:

Signature of Candidate **Signature of Co-Supervisor** **Signature of Supervisor**

KEY TO MASTERCHART

F	Female
PMB	Post-menopausal bleed
HMB	Heavy menstrual bleed
AUB	Abnormal uterine bleed
BPV	Bleeding per vaginum
DPV	Discharge per vaginum
Endo	Endometrial
LN	Lymph node
NA	Not applicable
Pos	Positive
Neg	Negative
Nuc	Nuclear
Memb	Membranous
LV	Lymphvascular
PN	Perineural
Add	Additional

S.no	Name	Age/Sex	MRD No.	C/P	Type of specimen	Gross						Microscopy								
						location	growth pattern	size	extension	myometrial involvement	add features	pattern	differentiation	mitosis	necrosis	myometrial involvement	solid component	extension	LV/PN invasion	parametrium
1	PLK	63/F	31520	PMB	hysterectomy with bso	endometrium	polypoidal	4x2x1.5 cm	fundus,body,isthmus, endocervix	<1/2	NA	glandular, villous	no	no	no	<1/2	<5%	fundus,body,isthmus, endocervix	no	free
2	BR	70/F	56921	PMB	hysterectomy with bso and omentum	endometrium	exophytic	3x2.5x1 cm	fundus,body,isthmus	>1/2	NA	glandular	no	no	no	>1/2	<5%	fundus,body,isthmus	no	free
3	GK	60/F	118883	PMB	hysterectomy with bso	endometrium	polypoidal	2.5X1X1 cm	fundus,body,isthmus	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body,isthmus	no	free
4	RK	42/F	130219	HMB	hysterectomy with bso	endometrium	polypoidal	4.5x1x1 cm	fundus,body,isthmus	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body,isthmus	no	free
5	NK	65/F	122762	PMB	hysterectomy with bso	endometrium	polypoidal	1.8x1x1 cm	fundus,body	<1/2	NA	glandular,sheets,nests	no	no	no	<1/2	>5%,<50%	fundus,body	no	free
6	DK	67/F	144872	PMB	hysterectomy with bso	endometrium	polypoidal	4.5X3.5X2 cm	fundus,body	<1/2	NA	glandular,sheets,nests	no	no	no	<1/2	>50%	fundus,body	no	free
7	SR	55/F	157057	AUB	hysterectomy with bso	endometrium	polypoidal	2.5X1X1 cm	fundus,body	<1/2	NA	glandular,sheets,nests	no	no	no	<1/2	>5%,<50%	fundus,body,isthmus	no	free
8	MK	59/F	93508	PMB	endo curettes	endometrium	NA	8x5x3 cm	NA	NA	NA	glandular	no	no	yes,<50%	NA	<5%	NA	no	NA
9	HK	55/F	146777	AUB	hysterectomy with bso and omentum	endometrium	polypoidal	7.5x5.5x6 cm	fundus,body,isthmus, endocervix	>1/2	NA	glandular,fascicles,nests	epithelial and mesenchymal	<5/10 hpf	no	>1/2	>50%	fundus,body,isthmus, endocervix	no	free
10	PD	70/F	102401	PMB	hysterectomy with bso	endometrium	polypoidal	7X5X2.5 cm	fundus,body	>1/2	NA	glandular,fascicles,nests	epithelial and mesenchymal	<5/10 hpf	no	>1/2	>50%	fundus,body	no	free
11	BR	70/F	36210	PMB	endo curettes	endometrium	NA	4.5X3.5X2 cm	NA	NA	NA	glandular	no	no	no	NA	>50%	NA	no	NA
12	UD	59/F	128495	PMB	endo curettes	endometrium	NA	0.8X0.6X0.4 cm	NA	NA	NA	sheets, nests	no	>5/10 hpf	yes,<50%	NA	>50%	NA	no	NA
13	NK	65/F	113851	PMB	endo curettes	endometrium	NA	4X3X1 cm	NA	NA	NA	sheets, nests, papillae	no	no	no	NA	>50%	NA	no	NA
14	KD	75/F	169644	PMB	endo curettes	endometrium	NA	1.8x1x1 cm	NA	NA	NA	sheets, nests, papillae	no	<5/10 hpf	yes	NA	>50%	NA	no	NA
15	HK	64/F	180928	PELVIC PAIN	hysterectomy with bso, vaginal cuff, b/l pelvic LN	cervix	exophytic	2.5x1.5x1 cm	posterior lip cervix	NA	NA	sheets, nests	no	no	no	NA	NA	cervix	no	free
16	GK	51/F	125092	BPV	hysterectomy with bso, upper 2/3 vagina, omentum, b/l pelvic LN , para aortic LN	cervix	exophytic	3.5x2.8x1 cm	cervix,body,isthmus,upper 2/3 vagina	>1/2	NA	sheets, nests	no	no	no	>1/2	NA	cervix,body,isthmus,vaginal vault	no	free

				FIGO Grade	pTNM	Histological Diagnosis	IHC if available												Final Diagnosis
adnexa	LN	omentum	add features				ER	PR	Napsin A	WT1	p53	p16	Ki-67	vimentin	SMA	desmin	CD10	others	
free	NA	NA	NA	I	T1aNxMx	ENDOMETRIOID CARCINOMA-VILLOGLANDULAR	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA-VILLOGLANDULAR
free	NA	free	senile cystic atrophy	I	T1bNxMx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	NA	NA	endometrial hyperplasia without atypia	I	T1aNxMx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	NA	NA	NA	I	T1aNxMx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	NA	NA	senile cystic atrophy	II	T1aNxMx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	NA	NA	endometrial hyperplasia without atypia	III	T1aNxMx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	NA	NA	NA	II	T1aNxMx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
NA	NA	NA	NA	I	NA	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	NA	free	NA	III	T1bN0Mx	MMMT	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	MMMT
free	NA	NA	senile cystic atrophy	III	T1bN0Mx	MMMT	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	MMMT
NA	NA	NA	senile cystic atrophy	III	NA	SEROUS CARCINOMA- HIGH GRADE	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	SEROUS CARCINOMA-HIGH GRADE
NA	NA	NA	NA	III	NA	SEROUS CARCINOMA- HIGH GRADE	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	SEROUS CARCINOMA-HIGH GRADE
NA	NA	NA	senile cystic atrophy	III	NA	SEROUS CARCINOMA- HIGH GRADE	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	SEROUS CARCINOMA-HIGH GRADE
NA	NA	NA	senile cystic atrophy	III	NA	SEROUS CARCINOMA- HIGH GRADE	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	SEROUS CARCINOMA-HIGH GRADE
free	free	NA	NA	NA	T1b1N0Mx	NON KERATINISING SCC	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NON KERATINISING SCC
free	free	free	NA	NA	T1b1N0Mx	KERATINISING SCC	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	KERATINISING SCC

S.no	Name	Age/Sex	MRD No.	C/P	Type of specimen	Gross						Microscopy								
						location	growth pattern	size	extension	myometrial involvement	add features	pattern	differentiation	mitosis	necrosis	myometrial involvement	solid component	extension	LV/PN invasion	parametrium
17	K	50/F	167161	BPV	cone biopsy	cervix	NA	1.5x1x0.6 cm	NA	NA	NA	sheets, nests	no	no	no	NA	NA	cervix	no	NA
18	PM	61/F	184885	PMB	hysterectomy with bso,omentum, b/l pelvic LN	endometrium	exophytic	3x2x2 cm	fundus,body,isthmus	>1/2	NA	glandular	no	no	no	>1/2	<5%	fundus,body,isthmus	no	free
19	VR	58/F	187299	PMB	hysterectomy with bso	endometrium	polypoidal	3.5X2.5X1.5 cm	fundus,body	<1/2	NA	glandular,sheets,nests	no	no	no	<1/2	>5%,<50%	fundus,body	no	free
20	RM	61/F	199519	PMB	hysterectomy with bso,b/l pelvic LN, para aortic LN	endometrium	exophytic	6x3.5x3 cm	fundus,body,isthmus, endocervix	>1/2	NA	glandular,sheets,nests	no	no	no	>1/2	>5%,<50%	fundus,body,isthmus, endocervix	no	free
21	MV	56/F	216873	PMB	hysterectomy with bso	endometrium	polypoidal	3X2X2 cm	fundus,body	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body	no	free
22	GK	66/F	206492	PMB	hysterectomy with bso	endometrium	polypoidal	1x1x1 cm	fundus,body	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body	no	free
23	K	57/F	222145	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	exophytic	5X2X1.5 cm	fundus,body,isthmus, endocervix	>1/2	NA	glandular, villous	no	no	no	>1/2	<5%	fundus,body,isthmus, endocervix	no	free
24	KJ	65/F	252440	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	exophytic	8x8x5 cm	fundus,body,isthmus, endocervix	>1/2	NA	glandular,sheets,nests	squamous	no	no	>1/2	>5%,<50%	fundus,body,isthmus, endocervix	no	free
25	PP	71/F	250855	PMB	hysterectomy with bso	endometrium	polypoidal	3.5X2.5X1.5 cm	fundus,body	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body	no	free
26	SK	52/F	270626	AUB	hysterectomy with bso	endometrium	polypoidal	2.5x1.5x1 cm	fundus,body	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body	no	free
27	SD	64/F	277314	PMB	hysterectomy with bso,omentum, b/l pelvic LN	endometrium	polypoidal	4x2x1.5 cm	fundus,body	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body	no	free
28	RK	56/F	284170	AUB	hysterectomy with bso,omentum, b/l pelvic LN	endometrium	exophytic	4.5X3.5X2 cm	fundus,body,isthmus	>1/2	NA	glandular	no	no	no	>1/2	<5%	fundus,body,isthmus	no	free
29	JK	54/F	292763	AUB	hysterectomy with bso, b/l pelvic LN	endometrium	polypoidal	2.5X1X1 cm	fundus,body,isthmus	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body,isthmus	no	free
30	RKA	56/F	311698	PMB	hysterectomy with bso,omentum, b/l pelvic LN	endometrium	exophytic	4.5X3.5X2 cm	fundus,body,isthmus, endocervix	>1/2	NA	glandular	no	no	no	>1/2	<5%	fundus,body,isthmus, endocervix	no	free

				FIGO Grade	pTNM	Histological Diagnosis	IHC if available												Final Diagnosis
adnexa	LN	omentum	add features				ER	PR	Napsin A	WT1	p53	p16	Ki-67	vimentin	SMA	desmin	CD10	others	
NA	NA	NA	NA	NA	NA	NON KERATINISING SCC	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NON KERATINISING SCC
free	free	free	endometrial hyperplasia without atypia	I	T1bN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	NA	NA	NA	II	T1aNxMx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	endometrial hyperplasia without atypia	II	T1bN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	NA	NA	NA	I	T1aNxMx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	NA	NA	atypical endometrial hyperplasia	I	T1aNxMx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	NA	I	T1bN0Mx	ENDOMETRIOID CARCINOMA-VILLOGLANDULAR	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA-VILLOGLANDULAR
free	free	NA	senile cystic atrophy	II	T1bN0Mx	ENDOMETRIOID CARCINOMA WITH SQUAMOUS DIFF	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA WITH SQUAMOUS DIFF
free	NA	NA	senile cystic atrophy	I	T1aNxMx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	NA	NA	NA	I	T1aNxMx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	free	NA	I	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	free	NA	I	T1bN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	atypical endometrial hyperplasia	I	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	free	NA	I	T1bN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA

S.no	Name	Age/Sex	MRD No.	C/P	Type of specimen	Gross						Microscopy								
						location	growth pattern	size	extension	myometrial involvement	add features	pattern	differentiation	mitosis	necrosis	myometrial involvement	solid component	extension	LV/PN invasion	parametrium
31	SM	61/F	320233	PMB	hysterectomy with bso,omentum, b/l pelvic LN	endometrium	exophytic	7X5X2.5 cm	fundus,body,isthmus, endocervix	>1/2	NA	glandular,sheets,nests	no	no	yes	>1/2	>5%,<50%	fundus,body,isthmus, endocervix	no	free
32	R	50/F	275499	AUB	hysterectomy with bso, b/l pelvic LN	endometrium	polypoidal	1.5x1x0.6 cm	fundus,body,isthmus, endocervix	<1/2	NA	glandular	no	no	yes	<1/2	<5%	fundus,body,isthmus, endocervix	no	free
33	MK	62/F	363643	PMB	hysterectomy with bso	endometrium	polypoidal	4.5X3.5X2 cm	fundus,body,isthmus	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body,isthmus	no	free
34	DS	59/F	364832	PMB	hysterectomy with bso	endometrium	exophytic	5X2X1.5 cm	fundus,body,isthmus	>1/2	NA	glandular,sheets,nests	no	no	no	>1/2	>5%,<50%	fundus,body,isthmus	no	free
35	MJ	52/F	365243	AUB	hysterectomy with bso, b/l pelvic LN	endometrium	exophytic	5X4X2 cm	fundus,body	>1/2	NA	glandular	no	no	no	>1/2	<5%	fundus,body	no	free
36	B	54/F	366572	AUB	hysterectomy with bso, b/l pelvic LN	endometrium	exophytic	2.5x1.5x1 cm	fundus,body	<1/2	NA	glandular, papillae	no	no	no	<1/2	NA	fundus,body	no	free
37	IR	72/F	356819	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	exophytic	6X6X3.5 cm	fundus,body	>1/2	NA	glandular,sheets,nests	no	no	no	>1/2	>50%	fundus,body	no	free
38	SK	59/F	377034	PMB	hysterectomy with bso	endometrium	exophytic	2.5x1.5x1 cm	fundus,body	>1/2	NA	glandular	no	no	no	>1/2	<5%	fundus,body	no	free
39	NK	61/F	364107	PMB	hysterectomy with bso	endometrium	exophytic	4X4X2.5 cm	fundus,body,isthmus, endocervix	>1/2	NA	glandular,sheets,nests	no	no	no	>1/2	>5%,<50%	fundus,body,isthmus, endocervix	LV +	free
40	SS	59/F	412179	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	exophytic	6X5.5X3 cm	fundus,body,isthmus, endocervix	>1/2	NA	glandular	no	no	no	>1/2	<5%	fundus,body,isthmus, endocervix	no	free
41	BD	76/F	169356	PMB	hysterectomy with bso	endometrium	polypoidal	5X4X2 cm	fundus,body,isthmus	>1/2	NA	glandular,sheets,fascicles	no	no	no	>1/2	>50%	fundus,body,isthmus	LV +	free
42	SK	70/F	1387	PMB	endo curettes	endometrium	NA	2.5x1.5x1 cm	NA	NA	NA	glandular	no	no	no	NA	<5%	endometrium	no	NA
43	MJ	51/F	250460	AUB	endo curettes	endometrium	NA	0.8X0.6X0.4 cm	NA	NA	NA	glandular	no	no	no	NA	<5%	endometrium	no	NA
44	TS	76/F	373870	PMB	endo curettes	endometrium	NA	1.5x1x0.6 cm	NA	NA	NA	glandular, papillae	no	no	no	NA	>50%	NA	no	NA

				FIGO Grade	pTNM	Histological Diagnosis	IHC if available												Final Diagnosis
adnexa	LN	omentum	add features				ER	PR	Napsin A	WT1	p53	p16	Ki-67	vimentin	SMA	desmin	CD10	others	
free	free	free	NA	II	T1bN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	NA	I	T1aN0Mx	ENDOMETRIOID CARCINOMA	pos	NA	NA	NA	NA	NA	30%	focal pos	NA	NA	NA	CK7-pos, CK20-neg	ENDOMETRIOID CARCINOMA
free	NA	NA	NA	I	T1aNxMx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	NA	NA	NA	II	T1bNxMx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	NA	NA	NA	I	T1bN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	endometrial hyperplasia without atypia	NA	T1aN0Mx	ADENOCARCINOMA	neg	NA	pos	neg	weak pos	neg	40%	NA	NA	NA	NA	CK7-pos, CK20-neg, beta catenin-neg	CLEAR CELL ADENOCARCINOMA
free	free	NA	atypical endometrial hyperplasia	III	T1bN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	NA	NA	senile cystic atrophy	I	T1bNxMx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	NA	NA	NA	II	T1bNxMx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	NA	I	T1bN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	NA	NA	senile cystic atrophy	III	T1bNxMx	DE-DIFFERENTIATED ENDOMETRIAL CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	DE-DIFFERENTIATED ENDOMETRIAL CARCINOMA
NA	NA	NA	senile cystic atrophy	I	NA	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
NA	NA	NA	NA	I	NA	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
NA	NA	NA	senile cystic atrophy	III	NA	SEROUS CARCINOMA- HIGH GRADE	pos	NA	neg	neg	NA	NA	80%	NA	NA	NA	NA	CK7 - pos, CK20-neg	SEROUS CARCINOMA-HIGH GRADE

S.no	Name	Age/Sex	MRD No.	C/P	Type of specimen	Gross						Microscopy								
						location	growth pattern	size	extension	myometrial involvement	add features	pattern	differentiation	mitosis	necrosis	myometrial involvement	solid component	extension	LV/PN invasion	parametrium
45	URP	65/F	255370	PMB	endo curettes	endometrium	NA	2.5X1X1 cm	NA	NA	NA	glandular	no	<5/10 hpf	yes	NA	<5%	endometrium	no	NA
46	SD	64/F	277314	PMB	endo curettes	endometrium	NA	2X1X0.8 cm	NA	NA	NA	glandular	no	no	no	NA	<5%	endometrium	no	NA
47	SK	45/F	286126	AUB	endo curettes	endometrium	NA	4.5X3.5X2 cm	NA	NA	NA	glandular	no	no	no	NA	<5%	endometrium	no	NA
48	KJ	56/F	275321	DPV	cervical biopsy	cervix	NA	2X1X0.8 cm	NA	NA	NA	sheets, nests	no	no	no	NA	NA	cervix	no	NA
49	SS	62/F	337729	PELVIC PAIN	hysterectomy with bso, b/l pelvic LN	cervix	exophytic	4X3X2 cm	cervix, isthmus	NA	NA	sheets, nests	no	no	no	NA	NA	cervix, isthmus	no	NA
50	HK	50/F	278655	AUB	hysterectomy with bso,omentum, b/l pelvic LN	endometrium	polypoidal	8x5x3 cm	fundus,body	>1/2	multiple intramural and subserosal fibroids	glandular,fascicles,nests	epithelial and mesenchymal	brisk	yes, <50%	>1/2	>50%	fundus,body	no	free
51	TK	23/F	216067	HMB	hysterectomy with bso	endometrium	polypoidal	9X8X6 cm	fundus,body,isthmus, endocervix, ectocervix	>1/2	NA	glandular,sheets,nests	no	<5/10 hpf	no	>1/2	NA	fundus,body,isthmus, endocervix, ectocervix	LV +	involved
52	LS	72/F	329644	PMB	hysterectomy with bso,omentum, b/l pelvic LN	intramural	nodular mass	6X6X3.5 cm	fundus,body,isthmus	>1/2	NA	sheets,fascicles	no	>10/10 hpf	yes,>50%	>1/2	NA	fundus,body,isthmus	no	free
53	HK	52/F	181254	BPV	hysterectomy with bso	no growth	NA	NA	NA	NA	NA	sheets, nests	no	no	no	NA	NA	endocervix	no	free
54	NK	53/F	251412	BPV	hysterectomy with bso, vaginal cuff, b/l pelvic LN	cervix	exophytic	4X3X2 cm	endocervix, isthmus	NA	NA	sheets, nests	no	no	no	NA	NA	cervix, isthmus	no	free
55	KK	60/F	256032	BPV	hysterectomy with bso, vaginal cuff, b/l pelvic LN	cervix	exophytic	4x2x1.5 cm	cervix, isthmus, body	NA	NA	sheets, nests	no	no	no	NA	NA	cervix, isthmus, body	no	free
56	PL	49/F	307221	PELVIC PAIN	hysterectomy with bso, b/l pelvic LN	cervix	exophytic	3X3X1 cm	cervix,body,isthmus	NA	NA	sheets, nests	no	no	no	NA	NA	cervix,body,isthmus	no	free
57	JK	60/F	281908	BPV	hysterectomy with bso, upper 1/3 vagina,b/l pelvic LN	no growth	NA	NA	NA	NA	NA	sheets, nests	no	no	no	NA	NA	cervix	no	free
58	GK	40/F	353981	PELVIC PAIN	hysterectomy with bso, b/l pelvic LN	cervix	exophytic	3.5X2.5X1.5 cm	cervix, isthmus	NA	NA	sheets, nests	no	no	no	NA	NA	cervix, isthmus	no	free
59	SK	70/F	370622	PMB	hysterectomy with bso, vaginal cuff, omentum,b/l pelvic LN	cervix	exophytic	1.8x1x1 cm	cervix, isthmus	NA	NA	glandular,sheets,nests	no	no	no	NA	NA	cervix, isthmus	no	free
60	BK	39/F	361374	DPV	hysterectomy with bso, vaginal cuff, b/l pelvic LN	cervix	exophytic	4.5X3.5X2 cm	cervix	NA	NA	sheets, nests	no	no	no	NA	NA	cervix	no	free
61	NK	85/F	396304	PMB	hysterectomy with bso	no growth	NA	NA	NA	NA	NA	sheets, nests	no	no	no	NA	NA	cervix	no	free
62	DK	57/F	389480	AUB	hysterectomy with bso, b/l pelvic LN	endometrium	exophytic	4x2x1.5 cm	fundus,body,isthmus	>1/2	NA	glandular,sheets,nests	no	no	no	>1/2	>5%,<50%	fundus,body,isthmus	no	free

				FIGO Grade	pTNM	Histological Diagnosis	IHC if available												Final Diagnosis
adnexa	**LN**	**omentum**	**add features**				**ER**	**PR**	**Napsin A**	**WT1**	**p53**	**p16**	**Ki-67**	**vimentin**	**SMA**	**desmin**	**CD10**	**others**	
NA	NA	NA	senile cystic atrophy	I	NA	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
NA	NA	NA	NA	I	NA	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
NA	NA	NA	NA	I	NA	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
NA	NA	NA	NA	NA	NA	NON KERATINISING SCC	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NON KERATINISING SCC
NA	free	NA	NA	NA	T1bN0Mx	NON KERATINISING SCC	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NON KERATINISING SCC
free	free	free	LM	NA	T1bN0Mx	MMMT	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	MMMT
free	NA	NA	NA	NA	T3bNxMx	ENDOMETRIAL STROMAL SARCOMA- LOW GRADE	pos	pos	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIAL STROMAL SARCOMA-LOW GRADE
free	NA	NA	NA	NA	T1bNxMx	LEIOMYOSARCOMA	neg	neg	NA	pos	NA	NA	NA	NA	pos	neg	neg	beta catenin-neg, CD34-neg	LEIOMYOSARCOMA
free	NA	NA	NA	NA	T1a1NxMx	ENDOCERVICAL ADENOCARCINOMA, USUAL TYPE	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOCERVICAL ADENOCARCINOMA, USUAL TYPE
free	free	NA	senile cystic hyperplasia	NA	T1b1N0Mx	NON KERATINISING SCC	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NON KERATINISING SCC
free	free	NA	NA	NA	T1b1N0Mx	NON KERATINISING SCC	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NON KERATINISING SCC
free	free	NA	NA	NA	T1b1N0Mx	NON KERATINISING SCC	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NON KERATINISING SCC
free	free	NA	senile cystic hyperplasia	NA	T1a2N0Mx	KERATINISING SCC	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	KERATINISING SCC
free	free	NA	NA	NA	T1b1N0Mx	NON KERATINISING SCC	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NON KERATINISING SCC
free	free	free	NA	NA	T1b1N0Mx	MUCINOUS CARCINOMA, INTESTINAL TYPE	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	MUCINOUS CARCINOMA, INTESTINAL TYPE
free	free	NA	NA	NA	T1b2N0Mx	KERATINISING SCC	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	KERATINISING SCC
free	NA	NA	NA	NA	T1a1N0Mx	NON KERATINISING SCC	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NON KERATINISING SCC
free	metastatic iliac LN	NA	NA	II	T1bN1Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA

S.no	Name	Age/Sex	MRD No.	C/P	Type of specimen	Gross						Microscopy								
						location	growth pattern	size	extension	myometrial involvement	add features	pattern	differentiation	mitosis	necrosis	myometrial involvement	solid component	extension	LV/PN invasion	parametrium
63	M	45/F	409830	AUB	hysterectomy	cervix	exophytic	2.5x1.5x1 cm	cervix, isthmus, body	NA	NA	glandular,sheets,nests	no	no	no	NA	NA	cervix, isthmus, body	no	free
64	SA	52/F	421477	AUB	hysterectomy with bso	endometrium	polypoidal	0.8X0.6X0.4 cm	fundus,body	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body	no	free
65	UR	57/F	4029	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	polypoidal	2X2X1 cm	fundus,body,isthmus	<1/2	NA	glandular	no	no	no	<1/2	>5%,<50%	fundus,body,isthmus	no	free
66	UR	65/F	420437	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	polypoidal	6x3.5x3 cm	fundus,body	>1/2	NA	glandular	no	no	no	>1/2	>50%	fundus,body	no	free
67	RK	53/F	417221	AUB	hysterectomy with bso, b/l pelvic LN	endometrium	exophytic	6X2X1.5 cm	fundus,body,isthmus, endocervix	>1/2	NA	glandular	no	no	no	>1/2	<5%	fundus,body,isthmus, endocervix	no	free
68	BK	75/F	441875	PMB	hysterectomy with bso	endometrium	polypoidal	4X3X2 cm	fundus,body	<1/2	NA	glandular,sheets,nests	no	no	no	<1/2	>5%,<50%	fundus,body	no	free
69	RR	72/F	439624	PMB	hysterectomy with bso	endometrium	exophytic	6X2X1.5 cm	fundus,body,isthmus	>1/2	NA	glandular	no	no	no	>1/2	<5%	fundus,body,isthmus	no	free
70	RS	60/F	448263	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	polypoidal	2.5x1.5x1 cm	fundus,body,isthmus	<1/2	NA	glandular,sheets,nests	no	no	no	<1/2	>5%,<50%	fundus,body,isthmus	no	free
71	JK	46/F	15918	HMB	hysterectomy with bso	endometrium	polypoidal	6x3.5x3 cm	fundus,body,isthmus	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body,isthmus	no	free
72	PS	58/F	443947	PMB	hysterectomy with bso, b/l iliac LN , para aortic LN	endometrium	polypoidal	4x2x1.5 cm	fundus,body	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body	no	free
73	S	76/F	446913	PMB	hysterectomy with bso,omentum,b/l pelvic LN	endometrium	polypoidal	4.5X3.5X2 cm	fundus,body,isthmus	<1/2	NA	glandular,sheets,nests	no	no	no	<1/2	>50%	fundus,body,isthmus	no	free
74	ND	48/F	461919	AUB	hysterectomy with bso	endometrium	exophytic	3.5X2.5X1.5 cm	fundus,body	>1/2	NA	glandular,sheets,nests	no	no	no	>1/2	>50%	fundus,body	no	free
75	TK	56/F	466335	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	exophytic	7X3X2 cm	fundus,body,isthmus, endocervix	>1/2	NA	glandular,sheets,nests	no	no	no	>1/2	>50%	fundus,body,isthmus, endocervix	no	free
76	BG	62/F	487802	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	polypoidal	3X1X1 cm	fundus,body,isthmus	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body,isthmus	no	free
77	SD	55/F	492359	AUB	hysterectomy with bso,omentum,b/l pelvic LN	endometrium	polypoidal	4X3X2 cm	fundus,body,isthmus, endocervix	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body,isthmus, endocervix	no	free

				FIGO Grade	pTNM	Histological Diagnosis	IHC if available												Final Diagnosis
adnexa	LN	omentum	add features				ER	PR	Napsin A	WT1	p53	p16	Ki-67	vimentin	SMA	desmin	CD10	others	
NA	NA	NA	NA	NA	T1b1NxMx	ADENOSQUAMOUS CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ADENOSQUAMOUS CARCINOMA
free	NA	NA	NA	I	T1aNxMx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	atypical endometrial hyperplasia	II	T1bN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	endometrial hyperplasia without atypia	III	T1bN0Mx	SEROUS CARCINOMA- HIGH GRADE	pos	neg	NA	neg	diffuse strong pos	NA	80%	NA	NA	NA	NA	CK7-pos, CK20-neg,PAX 8-pos,CDX 2- neg	SEROUS CARCINOMA-HIGH GRADE
free	free	NA	NA	I	T1bN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	endometrial hyperplasia without atypia	II	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	NA	NA	senile cystic atrophy	I	T1bNxMx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	NA	II	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	NA	NA	NA	I	T1aNxMx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	NA	I	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	senile cystic atrophy	III	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	NA	NA	NA	III	T1bNxMx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	NA	III	T1bN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	NA	I	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	NA	I	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA

S.no	Name	Age/Sex	MRD No.	C/P	Type of specimen	Gross						Microscopy								
						location	growth pattern	size	extension	myometrial involvement	add features	pattern	differentiation	mitosis	necrosis	myometrial involvement	solid component	extension	LV/PN invasion	parametrium
78	JK	54/F	480109	AUB	hysterectomy with bso	endometrium	polypoidal	1.5x1x0.6 cm	fundus,body,isthmus, endocervix	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body,isthmus, endocervix	no	free
79	UR	59/F	505647	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	polypoidal	3.5X2.5X1.5 cm	fundus,body	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body	no	free
80	BR	72/F	50279	PMB	hysterectomy with bso,omentum, b/l pelvic LN, para aortic LN	endometrium	exophytic	7X5X5 cm	fundus,body,isthmus, endocervix, parametrium	>1/2	NA	glandular, villous	no	no	no	>1/2	<5%	fundus,body,isthmus, endocervix,parametrium	no	involved
81	PS	60/F	509175	PMB	hysterectomy with bso, b/l pelvic LN , para aortic LN	endometrium	polypoidal	4.5X3.5X2 cm	fundus,body,isthmus	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body,isthmus	no	free
82	SB	55/F	500409	AUB	hysterectomy with bso,omentum, b/l pelvic LN	endometrium	polypoidal	4X3X2 cm	fundus,body,isthmus	<1/2	NA	glandular,sheets,nests	no	no	no	<1/2	>5%,<50%	fundus,body,isthmus	no	free
83	SK	70/F	521324	PMB	hysterectomy with bso,omentum, b/l pelvic LN, retroperitoneal LN	endometrium	exophytic	5X4X2 cm	fundus,body,isthmus	>1/2	NA	glandular,sheets,nests	no	no	no	>1/2	>5%,<50%	fundus,body,isthmus	no	free
84	RB	51/F	176714	AUB	hysterectomy with bso,omentum, b/l pelvic LN, para aortic LN	endometrium	polypoidal	4x2x1.5 cm	fundus,body,isthmus	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body,isthmus	no	free
85	SK	65/F	545539	PMB	hysterectomy with bso	endometrium	exophytic	8x5x3 cm	fundus,body,isthmus, endocervix	>1/2	NA	glandular,sheets,nests	no	no	no	>1/2	>5%,<50%	fundus,body,isthmus, endocervix	no	free
86	PR	39/F	558844	HMB	hysterectomy with bso,omentum, b/l pelvic LN	endometrium	polypoidal	2.5x1.5x1 cm	fundus,body	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body,isthmus	no	free
87	HPK	63/F	544749	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	exophytic	5X4X2 cm	fundus,body,isthmus, endocervix	>1/2	NA	glandular	no	no	no	>1/2	<5%	fundus,body,isthmus, endocervix, left fallopian tube	no	free
88	SK	46/F	3314	HMB	hysterectomy with bso	endometrium	polypoidal	3.5X2.5X1.5 cm	fundus,body,isthmus	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body,isthmus	no	free
89	SR	68/F	320162	PMB	hysterectomy with bso,omentum, b/l pelvic LN	endometrium	exophytic	4x2x1.5 cm	fundus,body,isthmus, endocervix	>1/2	NA	glandular	no	no	no	>1/2	<5%	fundus,body,isthmus, endocervix	no	free
90	KB	35/F	586249	HMB	hysterectomy with bso	endometrium	exophytic	3.5X2.5X1.5 cm	fundus,body,isthmus	>1/2	NA	glandular	no	no	no	>1/2	<5%	fundus,body,isthmus	no	free
91	PK	58/F	599520	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	exophytic	2.5x1.5x1 cm	fundus,body	>1/2	NA	glandular,sheets,nests	no	no	no	>1/2	>5%,<50%	fundus,body	no	free

				FIGO Grade	pTNM	Histological Diagnosis	IHC if available												Final Diagnosis
adnexa	LN	omentum	add features				ER	PR	Napsin A	WT1	p53	p16	Ki-67	vimentin	SMA	desmin	CD10	others	
free	NA	NA	NA	I	T1aNxMx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	NA	I	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	metastatic para aortic LN	free	endometrial hyperplasia without atypia	I	T3bN2Mx	ENDOMETRIOID CARCINOMA-VILLOGLANDULAR	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA-VILLOGLANDULAR
free	free	NA	NA	I	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	free	NA	II	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	free	senile cystic atrophy	II	T1bN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	free	senile cystic atrophy	I	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	NA	NA	senile cystic atrophy	II	T1bNxMx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	free	NA	I	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
involved	free	NA	NA	I	T3aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	NA	NA	NA	I	T1aNxMx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	free	senile cystic atrophy	I	T1bN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	atypical endometrial hyperplasia	II	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	NA	II	T1bN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA

S.no	Name	Age/Sex	MRD No.	C/P	Type of specimen	Gross						Microscopy								
						location	growth pattern	size	extension	myometrial involvement	add features	pattern	differentiation	mitosis	necrosis	myometrial involvement	solid component	extension	LV/PN invasion	parametrium
92	VR	59/F	278317	PMB	hysterectomy with bso, vaginal cuff, omentum,b/l pelvic LN	endometrium	polypoidal	2X2X1 cm	fundus,body,isthmus	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body,isthmus	no	free
93	AK	46/F	602044	HMB	hysterectomy with bso,omentum, b/l pelvic LN	endometrium	polypoidal	4x2x1.5 cm	fundus,body,isthmus	<1/2	NA	glandular,sheets,nests	no	no	no	<1/2	>5%,<50%	fundus,body,isthmus	no	free
94	SG	57/F	611171	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	exophytic	3.5X2.5X1.5 cm	fundus,body	>1/2	NA	glandular	no	no	no	>1/2	<5%	fundus,body	no	free
95	GS	50/F	622247	AUB	hysterectomy with bso, b/l pelvic LN	endometrium	polypoidal	3X3X1 cm	fundus,body	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body	no	free
96	PJ	52/F	625447	AUB	hysterectomy with bso	endometrium	polypoidal	5X4X2 cm	fundus,body,isthmus	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body,isthmus	no	free
97	MB	60/F	633257	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	polypoidal	3X1X1 cm	fundus,body,isthmus	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body,isthmus	no	free
98	N	60/F	1027705	PMB	hysterectomy with bso, b/l pelvic LN , para aortic LN	endometrium	exophytic	9X6.5X5 cm	fundus,body,isthmus	>1/2	NA	glandular,sheets,nests	squamous	no	yes	>1/2	>50%	fundus,body,isthmus	LV +	free
99	SDS	64/F	706205	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	exophytic	2.5x1.5x1 cm	fundus,body,isthmus	<1/2	NA	glandular,sheets,nests	no	yes	yes	>1/2	>50%	fundus,body,isthmus	no	free
100	GK	60/F	669678	PMB	hysterectomy with bso,omentum, b/l pelvic LN, para aortic LN	endometrium	polypoidal	2.5x1.5x1 cm	fundus,body,isthmus	>1/2	NA	glandular,sheets,nests	no	no	no	>1/2	>50%	fundus,body,isthmus	no	free
101	SS	73/F	866030	PMB	hysterectomy with bso,omentum, b/l pelvic LN	endometrium	polypoidal	4X3X2 cm	fundus,body	<1/2	NA	glandular, papillae,nests	no	<5/10 hpf	yes	<1/2	>50%	fundus,body	no	free
102	MD	65/F	999483	PMB	hysterectomy with bso	endometrium	polypoidal	5X4X2 cm	fundus,body,isthmus	>1/2	NA	glandular, papillae,nests	no	<5/10 hpf	yes	>1/2	>50%	fundus,body,isthmus	no	free
103	RK	53/F	417221	AUB	endo curettes	endometrium	NA	5X4X2 cm	NA	NA	NA	glandular	no	no	no	NA	<5%	NA	no	NA

				FIGO Grade	pTNM	Histological Diagnosis	IHC if available												Final Diagnosis
adnexa	**LN**	**omentum**	**add features**				**ER**	**PR**	**Napsin A**	**WT1**	**p53**	**p16**	**Ki-67**	**vimentin**	**SMA**	**desmin**	**CD10**	**others**	
free	free	free	endometrial hyperplasia without atypia	II	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	free	NA	II	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	NA	I	T1bN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	atypical endometrial hyperplasia	I	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	NA	NA	NA	I	T1aNxMx	ENDOMETRIOID CARCINOMA	weak pos	NA	NA	neg	NA	pos	NA	focal pos	NA	NA	NA	CK7 - pos, CK20- neg, PAX8- neg,CDX 2- neg	ENDOMETRIOID CARCINOMA
free	metastatic pelvic LN	NA	NA	I	T1aN1Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	NA	III	T1bN0Mx	DE-DIFFERENTIATED ENDOMETRIAL CARCINOMA	pos	pos	NA	neg	wild type pos	NA	NA	NA	NA	NA	neg	CK- pos, EMA- pos, CK8/18- pos, beta catenin-	DE-DIFFERENTIATED ENDOMETRIAL CARCINOMA
free	NA	NA	NA	III	T1bNxMx	SEROUS CARCINOMA- HIGH GRADE	focal pos	NA	neg	NA	diffuse strong pos	pos	85%	neg	NA	NA	neg	CK7 - pos, CK20- neg	SEROUS CARCINOMA-HIGH GRADE
involved	metastatic para aortic and pelvic LN	involved	NA	III	T3aN2Mx	SEROUS CARCINOMA- HIGH GRADE	pos	NA	neg	neg	diffuse strong pos	NA	80%	NA	NA	NA	NA	CK7 - pos, CK20- neg, PAX8- neg	SEROUS CARCINOMA-HIGH GRADE
free	free	free	senile cystic atrophy	III	T1aN1Mx	SEROUS CARCINOMA- HIGH GRADE	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	SEROUS CARCINOMA-HIGH GRADE
free	free	NA	senile cystic atrophy	III	T3aN0Mx	SEROUS CARCINOMA- HIGH GRADE	focal pos	NA	NA	neg	diffuse strong pos	NA	60%	NA	NA	NA	NA	CK7 - pos, CK20- neg, PAX8- pos, p40- neg	SEROUS CARCINOMA-HIGH GRADE
NA	NA	NA	NA	I	NA	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA

S.no	Name	Age/Sex	MRD No.	C/P	Type of specimen	Gross						Microscopy								
						location	growth pattern	size	extension	myometrial involvement	add features	pattern	differentiation	mitosis	necrosis	myometrial involvement	solid component	extension	LV/PN invasion	parametrium
104	AB	65/F	417516	PMB	endo curettes	endometrium	NA	1.5x1x0.6 cm	NA	NA	NA	glandular, papillae	no	no	no	NA	>50%	NA	no	NA
105	IK	60/F	482015	PMB	hysterectomy with bso	endometrium	polypoidal	2.5X1X1 cm	fundus,body	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body	no	free
106	RD	81/F	844697	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	exophytic	4x2x1.5 cm	fundus,body,isthmus	>1/2	NA	glandular	no	no	no	>1/2	<5%	fundus,body,isthmus	no	free
107	PK	63/F	914451	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	polypoidal	5X4X2 cm	fundus,body	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body	no	free
108	SK	65/F	490301	PMB	endo curettes	endometrium	NA	2.5X1X1 cm	NA	NA	NA	glandular	no	no	no	NA	<5%	NA	no	NA
109	GK	65/F	513914	PMB	endo curettes	endometrium	NA	3X1X1 cm	NA	NA	NA	glandular	no	no	no	NA	>50%	NA	no	NA
110	SG	55/F	535961	AUB	endo curettes	endometrium	NA	6x3.5x3 cm	NA	NA	NA	glandular	no	no	no	NA	<5%	NA	no	NA
111	S	64/F	573119	PMB	endo curettes	endometrium	NA	6X6X3.5 cm	NA	NA	NA	glandular	no	no	no	NA	<5%	NA	no	NA
112	PK	65/F	585202	PMB	endo curettes	endometrium	NA	6X5X1 cm	NA	NA	NA	glandular	no	no	no	NA	<5%	NA	no	NA
113	RK	45/F	576038	HMB	endo curettes	endometrium	NA	5X4X2 cm	NA	NA	NA	glandular	no	no	no	NA	>5%,<50%	NA	no	NA
114	KC	54/F	652644	AUB	endo curettes	endometrium	NA	6X5X1 cm	NA	NA	NA	glandular	no	no	no	NA	>5%,<50%	NA	no	NA
115	N	55/F	165587	AUB	endo curettes	endometrium	NA	3.5X2.5X1.5 cm	NA	NA	NA	glandular	no	<5/10 hpf	no	NA	<5%	NA	no	NA
116	SS	57/F	707045	PMB	endo curettes	endometrium	NA	4X3X2 cm	NA	NA	NA	glandular, papillae	no	<5/10 hpf	no	NA	<5%	NA	no	NA
117	M	62/F	705101	PMB	endo curettes	endometrium	NA	7X5X5 cm	NA	NA	NA	glandular, papillae	no	no	no	NA	<5%	NA	no	NA
118	RR	53/F	660458	AUB	endo curettes	endometrium	NA	5X4X2 cm	NA	NA	NA	glandular, papillae,nests	no	no	no	NA	>5%,<50%	NA	no	NA
119	SK	65/F	861350	PMB	endo curettes	endometrium	NA	0.5X0.4X0.2 cm	NA	NA	NA	glandular	no	no	no	NA	<5%	NA	no	NA
120	RD	65/F	440575	PMB	endo curettes	endometrium	NA	7X3X2 cm	NA	NA	NA	glandular, papillae,nests	no	<5/10 hpf	yes	NA	>50%	NA	no	NA
121	GK	63/F	681472	PMB	endo curettes	endometrium	NA	6x3.5x3 cm	NA	NA	NA	glandular,sheets,nests	epithelial and mesenchym	<5/10 hpf	yes, <50%	NA	>50%	NA	no	NA
122	SK	55/F	24197	PMB	endo curettes	endometrium	NA	1.5x1x0.6 cm	NA	NA	NA	glandular,fascicles,nests	epithelial and mesenchymal	>10/10hpf	no	NA	>50%	NA	no	NA

				FIGO Grade	pTNM	Histological Diagnosis	IHC if available												Final Diagnosis
adnexa	LN	omentum	add features				ER	PR	Napsin A	WT1	p53	p16	Ki-67	vimentin	SMA	desmin	CD10	others	
NA	NA	NA	senile cystic atrophy	III	NA	SEROUS CARCINOMA- HIGH GRADE	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	SEROUS CARCINOMA-HIGH GRADE
free	NA	NA	atypical endometrial hyperplasia	I	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	senile cystic atrophy	II	T1bN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	NA	I	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
NA	NA	NA	senile cystic atrophy	I	NA	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
NA	NA	NA	senile cystic atrophy	III	NA	ENDOMETRIOID CARCINOMA	pos	NA	NA	neg	NA	NA	NA	neg	NA	NA	NA	CK7 - pos, CK20-	ENDOMETRIOID CARCINOMA
NA	NA	NA	NA	I	NA	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
NA	NA	NA	NA	I	NA	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
NA	NA	NA	senile cystic atrophy	I	NA	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
NA	NA	NA	NA	II	NA	ENDOMETRIOID CARCINOMA	pos	NA	NA	neg	weak pos	NA	NA	NA	NA	NA	NA	CK7 - pos, CK20-	ENDOMETRIOID CARCINOMA
NA	NA	NA	NA	II	NA	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
NA	NA	NA	NA	I	NA	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
NA	NA	NA	NA	I	NA	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
NA	NA	NA	NA	I	NA	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	loss of MSH2 and	ENDOMETRIOID CARCINOMA
NA	NA	NA	NA	II	NA	ENDOMETRIOID CARCINOMA	pos	NA	neg	neg	weak pos	pos	60%	NA	NA	NA	NA	CK7 - pos, CK20- neg,	ENDOMETRIOID CARCINOMA
NA	NA	NA	atypical endometrial hyperplasia	I	NA	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
NA	NA	NA	senile cystic atrophy	III	NA	SEROUS CARCINOMA- HIGH GRADE	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	SEROUS CARCINOMA-HIGH GRADE
NA	NA	NA	NA	III	NA	MMMT	pos in epithelial	NA	neg	focal pos in epith	neg	NA	NA	pos in both	neg	pos in mesenchymal	NA	CK- pos in epithelia	MMMT
NA	NA	NA	NA	III	NA	MMMT	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	MMMT

S.no	Name	Age/Sex	MRD No.	C/P	Type of specimen	Gross						Microscopy								
						location	growth pattern	size	extension	myometrial involvement	add features	pattern	differentiation	mitosis	necrosis	myometrial involvement	solid component	extension	LV/PN invasion	parametrium
123	G	60/F	870763	PMB	endo curettes	endometrium	NA	2.5X1X1 cm	NA	NA	NA	glandular,sheets,nests	Epithelial,mesenchymal, chondroid	no	no	NA	>50%	NA	no	NA
124	GK	75/F	1000240	PMB	endo curettes	endometrium	NA	2.5X1X1 cm	NA	NA	NA	glandular,sheets,nests	epithelial and mesenchymal	<5/10 hpf	yes, <50%	NA	>50%	NA	no	NA
125	K	59/F	806403	PMB	Endo biopsy	endometrium	NA	1 cm	NA	NA	NA	Sheets	no	<5/10 hpf	yes, <50%	NA	NA	NA	no	NA
126	ND	23/F	980808	HMB	Endo biopsy	endometrium	NA	2cm	NA	NA	NA	sheets	no	<5/10 hpf	no	NA	NA	NA	no	NA
127	RM	45/F	543416	HMB	hysterectomy with bs	myometrium	polypoidal	6X5X1 cm	body	>1/2	NA	nests, lobules	no	<5/10 hpf	no	>1/2	NA	fundus,body	LV +	free
128	NR	42/F	727038	HMB	hysterectomy with bs	myometrium	polypoidal	4.5X3.5X2 cm	body	>1/2	single intramural fibroid	sheets, nests	no	<5/10 hpf	no	>1/2	NA	fundus,body	no	free
129	RG	38/F	706071	HMB	hysterectomy with bso	myometrium	polypoidal	5X4X2 cm	body	>1/2	NA	sheets, nests	no	>10/10 hpf	no	>1/2	NA	fundus,body	no	free
130	VJ	40/F	713716	AUB	hysterectomy with left fallopian tube	myometrium	polypoidal	6X5X1 cm	body	>1/2	multiple intramural fibroids	nests, lobules	smooth muscle	>5/10 hpf	yes, <50%	>1/2	NA	fundus,body	no	free
131	CK	33/F	792143	AUB	endo curettes	endometrium	NA	4x2x1.5 cm	NA	NA	NA	sheets, nests	no	<5/10 hpf	no	NA	NA	NA	no	NA
132	SS	45/F	926311	AUB	endo curettes	endometrium	NA	0.5X0.4X0.2 cm	NA	NA	NA	nests	no	<5/10 hpf	no	NA	NA	NA	no	NA
133	NS	55/F	489057	PMB	hysterectomy with bso	intramural	nodular mass	5X4X2 cm	fundus,body	>1/2	multiple intramural and subserosal fibroids	facicles	no	>10/10 hpf	yes	>1/2	NA	fundus,body	no	free
134	KG	39/F	676775	HMB	hysterectomy with bso	intramural	nodular mass	9X6.5X5 cm	fundus,body,isthmus	>1/2	NA	sheets, fascicles	no	>10/10 hpf	yes	<1/2	NA	fundus,body,isthmus	no	free

				FIGO Grade	pTNM	Histological Diagnosis	IHC if available												Final Diagnosis
adnexa	LN	omentum	add features				ER	PR	Napsin A	WT1	p53	p16	Ki-67	vimentin	SMA	desmin	CD10	others	
NA	NA	NA	NA	III	NA	MMMT	NA	NA	NA	cyto pos	NA	NA	NA	pos	NA	neg	NA	CK- neg, myogenin- neg	MMMT
NA	NA	NA	senile cystic atrophy	III	NA	MMMT	neg	NA	NA	neg	NA	NA	NA	pos in mesenchymal	neg	NA	neg	CK- pos in epithelial	MMMT
NA	NA	NA	NA	NA	NA	ENDOMETRIAL STROMAL SARCOMA- HIGH GRADE	neg	NA	NA	NA	NA	NA	95%	pos	NA	neg	focal pos	CK- focal weak pos, PAX8- focal pos	ENDOMETRIAL STROMAL SARCOMA- HIGH GRADE
NA	NA	NA	NA	NA	NA	ENDOMETRIAL STROMAL SARCOMA- HIGH GRADE	NA	neg	NA	NA	NA	NA	70%	NA	pos	neg	focal pos	cyclin D1- pos, h-caldesmon- neg	ENDOMETRIAL STROMAL SARCOMA- HIGH GRADE
free	NA	NA	NA	NA	T1bNxMx	ENDOMETRIAL STROMAL SARCOMA- LOW GRADE	pos	NA	NA	NA	NA	NA	1%	NA	neg	NA	diffuse positive	CK- neg, S-100- neg, CD34- neg,	ENDOMETRIAL STROMAL SARCOMA- LOW GRADE
free	NA	NA	LM	NA	T1aNxMx	ENDOMETRIAL STROMAL SARCOMA- LOW GRADE	pos	NA	NA	NA	NA	NA	5%	NA	neg	neg	diffuse positive	NA	ENDOMETRIAL STROMAL SARCOMA- LOW GRADE
free	NA	NA	NA	NA	T1aNxMx	ENDOMETRIAL STROMAL SARCOMA- LOW GRADE	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIAL STROMAL SARCOMA- LOW GRADE
free	NA	NA	LM	NA	T1bNxMx	ENDOMETRIAL STROMAL SARCOMA- LOW GRADE	pos	NA	NA	NA	NA	NA	25%	NA	pos	focal pos	diffuse positive	beta catenin- pos, cyclin d1- neg, CD117 -	ENDOMETRIAL STROMAL SARCOMA- LOW GRADE
NA	NA	NA	NA	NA	NA	ENDOMETRIAL STROMAL SARCOMA- LOW GRADE	pos	pos	NA	NA	NA	NA	6%	NA	pos	focal pos	diffuse positive	CK- neg, CD117- neg	ENDOMETRIAL STROMAL SARCOMA- LOW GRADE
NA	NA	NA	NA	NA	NA	ENDOMETRIAL STROMAL SARCOMA- LOW GRADE	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIAL STROMAL SARCOMA- LOW GRADE
free	NA	NA	LM	NA	T1aNxMx	LEIOMYOSARCOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	LEIOMYOSARCOMA
free	NA	NA	NA	NA	T1bNxMx	LEIOMYOSARCOMA	pos	NA	NA	NA	NA	NA	40%	pos	pos	pos	neg	S-100- neg, CD34- neg	LEIOMYOSARCOMA

S.no	Name	Age/Sex	MRD No.	C/P	Type of specimen	Gross						Microscopy								
						location	growth pattern	size	extension	myometrial involvement	add features	pattern	differentiation	mitosis	necrosis	myometrial involvement	solid component	extension	LV/PN invasion	parametrium
135	MB	48/F	775001	AUB	hysterectomy with bso, b/l pelvic LN	intramural	nodular mass	20X10X5 cm	fundus,body,isthmus	>1/2	NA	facicles	no	>10/10 hpf	yes,>50%	>1/2	NA	fundus,body,isthmus	LV +	involved
136	PK	64/F	839887	PMB	hysterectomy with bso, b/l pelvic LN	intramural	nodular mass	13X8X5 cm	fundus,body,isthmus	<1/2	multiple intramural and subserosal fibroids	glandular	no	>10/10 hpf	yes,>50%	>1/2	NA	fundus,body,isthmus	no	free
137	NB	51/F	1079317	AUB	hysterectomy with bso,omentum, b/l pelvic LN	intramural	nodular mass	7X3X2 cm	fundus,body,isthmus	>1/2	single intramural fibroid	sheets, fascicles	no	>10/10 hpf	yes,<50%	>1/2	NA	fundus,body,isthmus	no	free
138	PS	64/F	442304	PMB	hysterectomy with bso,omentum, b/l pelvic LN, retroperitoneal LN	endometrium	polypoidal	6X5X1 cm	fundus,body,isthmus	>1/2	NA	glandular,sheets,nests	epithelial and mesenchymal	no	no	>1/2	>50%	fundus,body,isthmus	no	free
139	AK	62/F	634722	PMB	hysterectomy with bso,omentum, b/l pelvic LN, para aortic LN	endometrium	polypoidal	6X5X1 cm	fundus,body,isthmus	>1/2	NA	glandular,fascicles,nests	epithelial ,mesenchymal, cartilagenous, osteoid	no	no	>1/2	>50%	fundus,body,isthmus	no	free
140	JA	72/F	676362	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	polypoidal	9X6.5X5 cm	fundus,body,isthmus, endocervix	>1/2	NA	glandular,fascicles,nests	epithelial and mesenchymal	no	no	>1/2	>50%	fundus,body,isthmus, endocervix	no	free
141	SL	50/F	725650	AUB	hysterectomy with bso, b/l pelvic LN	endometrium	polypoidal	10X6X3.5 cm	fundus,body,isthmus, endocervix	>1/2	NA	glandular,fascicles,nests	epithelial ,mesenchymal,rhabdoid, cartilagenous, osteoid	no	no	>1/2	>50%	fundus,body,isthmus, endocervix	no	free
142	KK	42/F	683381	HMB	hysterectomy with bso,omentum, b/l pelvic LN	endometrium	polypoidal	7X5X5 cm	fundus,body,isthmus	>1/2	NA	glandular, papillae,sheets	Epithelial,mesenchymal, chondroid	no	no	>1/2	>50%	fundus,body,isthmus	no	involved
143	JKS	64/F	847117	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	polypoidal	7X3X2 cm	fundus,body,isthmus, endocervix	>1/2	NA	glandular,sheets,nests	epithelial ,mesenchymal, cartilagenous, osteoid	no	no	>1/2	>50%	fundus,body,isthmus, endocervix	no	involved
144	UK	61/F	866165	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	polypoidal	7X3X1.8 cm	fundus,body,isthmus	>1/2	single intramural fibroid	glandular,sheets,nests	epithelial and mesenchymal	>10/10 hpf	yes,<50%	>1/2	>50%	fundus,body,isthmus	no	free
145	KK	66/F	6742	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	polypoidal	2.5x1.5x1 cm	fundus,body,isthmus	<1/2	multiple intramural fibroids	glandular,sheets,nests	epithelial and mesenchymal	>10/10 hpf	no	<1/2	>50%	fundus,body,isthmus	no	free

				FIGO Grade	pTNM	Histological Diagnosis	IHC if available												Final Diagnosis
adnexa	**LN**	**omentum**	**add features**				**ER**	**PR**	**Napsin A**	**WT1**	**p53**	**p16**	**Ki-67**	**vimentin**	**SMA**	**desmin**	**CD10**	**others**	
involved	NA	NA	NA	NA	T2bNxMx	LEIOMYOSARCOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	LEIOMYOSARCOMA
free	free	NA	LM	NA	T1bN0Mx	LEIOMYOSARCOMA	NA	NA	NA	NA	NA	NA	35%	pos	pos	pos	NA	CK - focal pos, S-100- neg,	LEIOMYOSARCOMA
free	free	free	LM	NA	T1bN0Mx	LEIOMYOSARCOMA	NA	NA	NA	NA	NA	NA	NA	NA	pos	pos	neg	CK - focal pos, h-Caldesm	LEIOMYOSARCOMA
free	free	free	NA	III	T1bN0Mx	MMMT	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	MMMT
free	free	free	NA	III	T1bN0Mx	MMMT	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	MMMT
free	metastatic pelvic LN	NA	senile cystic atrophy	III	T1bN0Mx	MMMT	focal pos in epithelial	NA	neg	neg	pos	NA	90%	diffuse pos in mesenchymal, focal pos in	focal pos in mesenchymal	pos in mesenchymal	NA	CK- pos in epithelial, S-100- neg	MMMT
free	free	NA	NA	III	T1bN0Mx	MMMT	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	MMMT
involved	metastatic pelvic LN	involved	NA	III	T3bN1Mx	MMMT	neg	NA	NA	neg	pos	pos	90%	NA	NA	NA	NA	CK - pos in epithelial, CK7 - pos	MMMT
free	metastatic pelvic LN	NA	NA	III	T3bN1Mx	MMMT	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	MMMT
free	NA	NA	LM	III	T1bN0Mx	MMMT	diffuse pos	diffuse pos	NA	neg	pos	NA	NA	pos in both	NA	NA	neg	CK- pos in epithelial, PAX8- diffuse	MMMT
free	free	NA	LM	III	T1aN0Mx	MMMT	pos in epithelial	pos in epithelial	NA	neg	NA	NA	NA	pos in mesenchymal	neg	neg	neg	CK- pos in epithelial, cyclin D1- neg	MMMT

S.no	Name	Age/Sex	MRD No.	C/P	Type of specimen	Gross						Microscopy								
						location	growth pattern	size	extension	myometrial involvement	add features	pattern	differentiation	mitosis	necrosis	myometrial involvement	solid component	extension	LV/PN invasion	parametrium
146	M	67/F	148937	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	polypoidal	2X2X1 cm	fundus,body,isthmus	<1/2	multiple intramural and subserosal fibroids	glandular,sheets,nests	epithelial and mesenchymal	>10/10 hpf	no	<1/2	>50%	fundus,body,isthmus	no	free
147	KD	58/F	988391	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	polypoidal	3X3X1 cm	fundus,body	>1/2	NA	glandular,sheets,nests	Epithelial,mesenchymal, rhabdoid	<5/10 hpf	no	>1/2	>50%	fundus,body	no	free
148	SS	60/F	1028709	PMB	hysterectomy with bso, b/l pelvic LN , para aortic LN	endometrium	polypoidal	3.5X2.5X1.5 cm	fundus,body,isthmus	<1/2	NA	glandular,fascicles,nests	Epithelial,mesenchymal, rhabdoid	<5/10 hpf	yes,<50%	<1/2	>50%	fundus,body,isthmus	no	free
149	BK	73/F	644032	PMB	hysterectomy with bso, b/l pelvic LN , para aortic LN	endometrium	polypoidal	4x2x1.5 cm	fundus,body,isthmus	<1/2	NA	glandular	no	no	no	<1/2	>5%,<50%	fundus,body,isthmus	no	free
150	LN	56/F	659012	AUB	hysterectomy with bso, b/l pelvic LN , para aortic LN	endometrium	polypoidal	5X4X2 cm	fundus,body,isthmus	<1/2	NA	glandular,sheets,nests	no	no	no	<1/2	>5%,<50%	fundus,body,isthmus	no	free
151	SD	59/F	657858	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	exophytic	4X3X2 cm	fundus,body,isthmus	>1/2	NA	glandular,sheets,nests	no	no	no	>1/2	>5%,<50%	fundus,body,isthmus	no	free
152	DK	55/F	664193	AUB	hysterectomy with bso, b/l pelvic LN	endometrium	exophytic	4X3X2 cm	fundus,body,isthmus, endocervix	>1/2	NA	glandular,sheets,nests	no	no	no	>1/2	>5%,<50%	fundus,body,isthmus, endocervix	no	free
153	MS	62/F	705101	PMB	hysterectomy with bso,omentum, b/l pelvic LN	endometrium	polypoidal	7X3X2 cm	fundus,body,isthmus, endocervix	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body,isthmus, endocervix	no	free
154	MKS	80/F	714628	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	exophytic	2.5x1.5x1 cm	fundus,body,isthmus	>1/2	NA	glandular,sheets,nests	no	no	no	>1/2	<5%	fundus,body,isthmus	no	free
155	HK	54/F	714271	AUB	hysterectomy with bso, b/l pelvic LN	endometrium	polypoidal	4x2x1.5 cm	fundus,body,isthmus	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body,isthmus	no	free
156	DS	76/F	332524	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	polypoidal	2.5x1.5x1 cm	fundus,body	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body,isthmus	no	free
157	HK	61/F	728808	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	polypoidal	3.5X2.5X1.5 cm	fundus,body	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body	no	free
158	HK	56/F	734692	AUB	hysterectomy with bso, b/l pelvic LN	endometrium	polypoidal	2.5x1.5x1 cm	fundus,body	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body	no	free
159	AKW	80/F	742402	PMB	hysterectomy with bso	endometrium	exophytic	6x3.5x3 cm	fundus,body,isthmus	>1/2	NA	glandular	no	no	no	>1/2	<5%	fundus,body,isthmus	no	free
160	MK	54/F	806682	AUB	hysterectomy with bso, b/l pelvic LN , para aortic LN	endometrium	exophytic	4.5X3.5X2 cm	fundus,body,isthmus	>1/2	NA	glandular	no	no	no	>1/2	<5%	fundus,body,isthmus	no	free

				FIGO Grade	pTNM	Histological Diagnosis	IHC if available												Final Diagnosis
adnexa	LN	omentum	add features				ER	PR	Napsin A	WT1	p53	p16	Ki-67	vimentin	SMA	desmin	CD10	others	
free	free	NA	LM	III	T1aN0Mx	MMMT	pos in epithelial	NA	NA	neg	NA	NA	NA	pos in mesenchymal	NA	NA	NA	CK - pos in epithelial	MMMT
free	metastatic pelvic LN	NA	NA	III	T1bN1Mx	MMMT	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	MMMT
free	free	NA	NA	III	T1aN0Mx	MMMT	neg	focal pos in epithelial	NA	cyto pos in mesenchymal	NA	NA	NA	diffuse pos in mesenchymal, focal	NA	NA	NA	CK- pos in epithelial,	MMMT
free	free	NA	senile cystic atrophy	II	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	metastatic para aortic LN	NA	NA	II	T1bN2Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	atypical endometrial hyperplasia	II	T1bN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	NA	II	T1bN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	free	NA	I	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	metastatic pelvic LN	NA	endometrial hyperplasia without atypia	I	T1bN1Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	NA	I	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	senile cystic atrophy	I	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	NA	I	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	NA	I	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	senile cystic atrophy	I	T1bN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	NA	I	T1bN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA

S.no	Name	Age/Sex	MRD No.	C/P	Type of specimen	Gross						Microscopy								
						location	growth pattern	size	extension	myometrial involvement	add features	pattern	differentiation	mitosis	necrosis	myometrial involvement	solid component	extension	LV/PN invasion	parametrium
161	HKD	65/F	730666	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	exophytic	4X3X2 cm	fundus,body,isthmus	>1/2	NA	glandular	no	no	no	>1/2	<5%	fundus,body,isthmus	no	free
162	MK	55/F	828457	AUB	hysterectomy with bso, b/l pelvic LN	endometrium	exophytic	3.5X2.5X1.5 cm	fundus,body,isthmus	>1/2	NA	glandular	no	no	no	>1/2	<5%	fundus,body,isthmus	no	free
163	RD	81/F	844697	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	exophytic	4x2x1.5 cm	fundus,body,isthmus	>1/2	NA	glandular	no	no	no	>1/2	<5%	fundus,body,isthmus	no	free
164	JK	65/F	489046	PMB	hysterectomy with bso and omentum	endometrium	exophytic	4X3X2 cm	fundus,body	>1/2	NA	glandular	no	no	no	>1/2	<5%	fundus,body	no	free
165	NB	65/F	845676	PMB	hysterectomy with bso, b/l pelvic LN , para aortic LN	endometrium	exophytic	5X4X2 cm	fundus,body	>1/2	NA	glandular	no	no	no	>1/2	<5%	fundus,body	no	free
166	SK	58/F	866010	AUB	hysterectomy with bso,omentum, b/l pelvic LN	endometrium	polypoidal	5X3X2 cm	fundus,body,isthmus	<1/2	NA	glandular,sheets,nests	no	no	no	<1/2	>5%,<50%	fundus,body,isthmus	no	free
167	N	59/F	869469	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	exophytic	4X3X2 cm	fundus,body	>1/2	NA	glandular,sheets,nests	no	no	no	<1/2	>5%,<50%	fundus,body	no	free
168	SK	65/F	861350	PMB	hysterectomy with bso, b/l iliac LN	endometrium	polypoidal	1.8x1x0.6 cm	fundus,body,isthmus	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body,isthmus	no	free
169	JK	58/F	891201	AUB	hysterectomy with bso, b/l pelvic LN	endometrium	exophytic	7X3X2 cm	fundus,body,isthmus, endocervix	>1/2	NA	glandular	no	no	no	>1/2	<5%	fundus,body,isthmus, endocervix	no	free
170	KR	72/F	904457	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	exophytic	2.5x1.5x1 cm	fundus,body	>1/2	NA	glandular	no	no	no	>1/2	<5%	fundus,body	no	free
171	PK	63/F	914451	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	polypoidal	5X4X2 cm	fundus,body	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body	no	free
172	MS	57/F	925744	AUB	hysterectomy with bso,omentum, b/l pelvic LN	endometrium	polypoidal	2.5x1.5x1 cm	fundus,body,isthmus	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body,isthmus	no	free
173	BR	68/F	928566	PMB	hysterectomy with bso,omentum, b/l pelvic LN	endometrium	polypoidal	4x2x1.5 cm	fundus,body,isthmus	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body,isthmus	no	free
174	JK	65/F	588412	PMB	hysterectomy with bso,omentum, b/l pelvic LN	endometrium	polypoidal	4X3X2 cm	fundus,body,isthmus	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body,isthmus	no	free
175	PK	60/F	948529	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	exophytic	6X3X1 cm	fundus,body,isthmus	>1/2	NA	glandular	no	no	no	>1/2	<5%	fundus,body,isthmus	no	free
176	BK	65/F	967818	PMB	hysterectomy with bso	endometrium	exophytic	3.5X2.5X1.5 cm	fundus,body	>1/2	NA	glandular, villous	no	no	no	>1/2	<5%	fundus,body	no	free

				FIGO Grade	pTNM	Histological Diagnosis	IHC if available												Final Diagnosis
adnexa	LN	omentum	add features				ER	PR	Napsin A	WT1	p53	p16	Ki-67	vimentin	SMA	desmin	CD10	others	
free	free	NA	senile cystic atrophy	I	T1aN0Mx	ENDOMETRIOID CARCINOMA	pos	NA	NA	neg	weak pos	NA	NA	NA	NA	NA	NA	CK-neg,MMR PROFICIENT	ENDOMETRIOID CARCINOMA
free	free	NA	NA	I	T1bN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	senile cystic atrophy	I	T1bN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	senile cystic atrophy	I	T1bN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	senile cystic atrophy	I	T1bN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	free	NA	II	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	atypical endometrial hyperplasia	II	T1bN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	NA	NA	atypical endometrial hyperplasia	I	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	NA	I	T1bN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	senile cystic atrophy	I	T1bN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	NA	I	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	free	atypical endometrial hyperplasia	I	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	free	senile cystic atrophy	I	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	free	senile cystic atrophy	I	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	NA	I	T1bN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	NA	NA	senile cystic atrophy	I	T1bN0Mx	ENDOMETRIOID CARCINOMA-VILLOGLANDULAR	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA-VILLOGLANDULAR

S.no	Name	Age/Sex	MRD No.	C/P	Type of specimen	Gross						Microscopy								
						location	growth pattern	size	extension	myometrial involvement	add features	pattern	differentiation	mitosis	necrosis	myometrial involvement	solid component	extension	LV/PN invasion	parametrium
177	MK	74/F	983628	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	polypoidal	2.5X1X1 cm	fundus,body,isthmus	<1/2	NA	glandular,sheets,nests	no	no	no	<1/2	<5%	fundus,body,isthmus	no	free
178	ML	70/F	70970	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	exophytic	5X3X2 cm	fundus,body,isthmus	>1/2	NA	glandular,sheets,nests	no	no	no	>1/2	>50%	fundus,body,isthmus	no	free
179	SKJ	66/F	233085	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	polypoidal	2.5x1.5x1 cm	fundus,body	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body,isthmus	no	free
180	SK	52/F	1048577	AUB	hysterectomy with bso,omentum, b/l pelvic LN	endometrium	polypoidal	2.5x1.5x1 cm	fundus,body,isthmus	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body,isthmus	no	free
181	SDK	46/F	1058466	AUB	hysterectomy with bso,omentum, b/l pelvic LN, para aortic LN	endometrium	exophytic	4X3X2 cm	fundus,body,isthmus	>1/2	NA	glandular	no	no	no	>1/2	<5%	fundus,body,isthmus	no	free
182	HK	30/F	1066349	HMB	hysterectomy with bso, b/l pelvic LN	endometrium	polypoidal	1.5x1x0.6 cm	fundus,body	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body,isthmus	no	free
183	SK	50/F	1082027	AUB	hysterectomy with bso, b/l pelvic LN	endometrium	exophytic	5X3X2 cm	fundus,body,isthmus	>1/2	NA	glandular	no	no	no	>1/2	<5%	fundus,body,isthmus	no	free
184	KD	66/F	297340	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	polypoidal	4.5X3.5X2 cm	fundus,body,isthmus	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body,isthmus	no	free
185	KK	40/F	7505	PELVIC PAIN	hysterectomy with bso	no growth	NA	NA	NA	NA	NA	sheets, nests	no	no	no	NA	NA	cervix	no	free
186	RK	50/F	448219	BPV	hysterectomy with bso	cervix	exophytic	5X4X2 cm	cervix, isthmus, body	NA	NA	sheets, nests	no	<5/10 hpf	no	NA	NA	cervix, isthmus, body	no	involved
187	JK	51/F	442100	PELVIC PAIN	hysterectomy with bso, vaginal cuff, b/l pelvic LN	cervix	exophytic	4.5X3.5X2 cm	cervix, isthmus	NA	NA	sheets, nests	no	no	no	NA	NA	cervix, isthmus	no	free
188	CK	40/F	507240	DPV	hysterectomy with bso, b/l pelvic LN	cervix	exophytic	1.5x1x0.6 cm	cervix	NA	NA	sheets, nests	no	no	no	NA	NA	cervix	no	free
189	SK	78/F	592305	BPV	hysterectomy with bso and omentum	no growth	NA	NA	NA	NA	NA	glandular, papillae	no	no	no	NA	NA	cervix	no	free
190	UD	55/F	648833	PELVIC PAIN	cervical biopsy	cervix	NA	4X3X2 cm	NA	NA	NA	sheets, nests	no	no	no	NA	NA	cervix	no	NA
191	BG	65/F	643803	BPV	hysterectomy with bso, b/l pelvic LN , para aortic LN	cervix	exophytic	7X5X3 cm	fundus,body,isthmus,cervix	NA	NA	sheets, nests	no	no	yes	NA	NA	fundus,body,isthmus	LV +	free
192	RK	66/F	782031	PMB	hysterectomy with bso,omentum, b/l pelvic LN	cervix	exophytic	3X1X1 cm	fundus,body,isthmus, endocervix	<1/2	NA	glandular, papillae,nests	no	no	no	<1/2	NA	fundus,body,isthmus, endocervix	no	free

				FIGO Grade	pTNM	Histological Diagnosis	IHC if available												Final Diagnosis
adnexa	**LN**	**omentum**	**add features**				**ER**	**PR**	**Napsin A**	**WT1**	**p53**	**p16**	**Ki-67**	**vimentin**	**SMA**	**desmin**	**CD10**	**others**	
free	free	NA	senile cystic atrophy	II	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	senile cystic atrophy	III	T1bN0Mx	ENDOMETRIOID CARCINOMA	focal pos	neg	NA	neg	focal pos	focal pos	90%	weak pos	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	senile cystic atrophy	I	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	free	NA	I	T1aN0Mx	ENDOMETRIOID CARCINOMA	pos	pos	NA	neg	neg	diffuse pos	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
involved	metastatic para aortic and pelvic LN	free	NA	I	T3aN2Mx	ENDOMETRIOID CARCINOMA	pos	pos	focal pos	neg	focal pos	patchy pos	NA	focal pos	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	NA	NA	NA	I	T1aN0Mx	ENDOMETRIOID CARCINOMA	diffuse pos	diffuse pos	NA	NA	wild type pos	patchy pos	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	metastatic pelvic LN	NA	NA	I	T1bN1Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	NA	NA	senile cystic atrophy	I	T1aN0Mx	ENDOMETRIOID CARCINOMA	diffuse pos	diffuse pos	NA	neg	wild type pos	patchy pos	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	NA	NA	NA	NA	T1a2NxMx	NON KERATINISING SCC	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NON KERATINISING SCC
free	NA	NA	NA	NA	T2b2NxMx	NON KERATINISING SCC	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NON KERATINISING SCC
free	free	NA	NA	NA	T1b2N0Mx	NON KERATINISING SCC	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NON KERATINISING SCC
free	free	NA	NA	NA	T1b1N0Mx	NON KERATINISING SCC	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NON KERATINISING SCC
free	NA	free	NA	NA	T1a1NxMx	ENDOCERVICAL ADENOCARCINOMA, USUAL TYPE	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOCERVICAL ADENOCARCINOMA, USUAL TYPE
NA	NA	NA	NA	NA	NA	NON KERATINISING SCC	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NON KERATINISING SCC
free	free	NA	senile cystic hyperplasia	NA	T1b2N0Mx	NON KERATINISING SCC	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NON KERATINISING SCC
free	free	free	NA	NA	T1aN0Mx	NON KERATINISING SCC	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NON KERATINISING SCC

S.no	Name	Age/Sex	MRD No.	C/P	Type of specimen	Gross						Microscopy								
						location	growth pattern	size	extension	myometrial involvement	add features	pattern	differentiation	mitosis	necrosis	myometrial involvement	solid component	extension	LV/PN invasion	parametrium
193	KK	44/F	769520	DPV	cervical biopsy	cervix	NA	2.5X1X1 cm	NA	NA	NA	glandular, papillae	no	no	no	NA	NA	cervix	no	NA
194	R	58/F	851660	BPV	cervical biopsy	cervix	NA	4x2x1.5 cm	NA	NA	NA	sheets, nests	no	no	no	NA	NA	cervix	no	NA
195	SK	32/F	856757	PELVIC PAIN	hysterectomy with bso, vaginal cuff, b/l pelvic LN	cervix	exophytic	5X3X2 cm	cervix	NA	NA	sheets, nests	no	no	no	NA	NA	cervix	no	free
196	RK	44/F	870763	BPV	hysterectomy with bso	no growth	endophytic	NA	NA	NA	NA	sheets, nests	no	no	no	NA	NA	cervix	no	free
197	SK	53/F	919946	BPV	cone biopsy	cervix	NA	1.5x1x0.6 cm	NA	NA	NA	sheets, nests	no	no	no	NA	NA	cervix	no	NA
198	AS	63/F	953116	BPV	hysterectomy with bso, b/l pelvic LN	cervix	exophytic	5X4X2 cm	cervix, isthmus	NA	NA	sheets, nests	no	no	no	NA	NA	cervix, isthmus	no	free
199	KK	41/F	989546	DPV	hysterectomy with bso, b/l pelvic LN	cervix	exophytic	1.5x1x0.6 cm	cervix	NA	NA	glandular,sheets,nests	no	no	no	NA	NA	cervix	no	free
200	KV	75/F	1091739	PELVIC PAIN	cervical biopsy	cervix	NA	0.8X0.6X0.4 cm	NA	NA	NA	sheets, nests	no	no	no	NA	NA	cervix	no	NA
201	NO	69/F	979303	BPV	hysterectomy with bso	no growth	endophytic	NA	NA	NA	NA	sheets, nests	no	no	no	NA	NA	endocervix	no	free
202	DD	62/F	1017028	PMB	hysterectomy with bso	endometrium	polypoidal	3.5X2.5X1.5 cm	fundus,body,isthmus, endocervix	<1/2	NA	glandular, papillae,sheets	no	no	no	<1/2	>5%,<50%	fundus,body,isthmus, endocervix	no	free
203	HMK	68/F	1028463	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	polypoidal	6x3.5x3 cm	fundus,body	<1/2	NA	glandular,sheets,nests	no	no	no	<1/2	>5%,<50%	fundus,body	no	free
204	PK	78/F	1028444	PMB	hysterectomy with bso,omentum, b/l pelvic LN, para aortic LN	endometrium	exophytic	4.5X3.5X2 cm	fundus,body,isthmus	>1/2	NA	glandular,sheets,nests	no	no	no	>1/2	>5%,<50%	fundus,body,isthmus	no	free
205	RM	45/F	592834	AUB	hysterectomy with bso, b/l pelvic LN	endometrium	polypoidal	1.8x1x0.6 cm	fundus,body	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body	no	free
206	RD	77/F	1079443	PMB	hysterectomy with bso	endometrium	polypoidal	2X2X1 cm	fundus,body	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body	no	free
207	L	38/F	7064	HMB	cervical biopsy	cervix	NA	0.5X0.4X0.2 cm	NA	NA	NA	sheets, nests	no	no	no	NA	NA	cervix	no	NA
208	AK	38/F	996887	BPV	cervical biopsy	cervix	NA	2.5X1X1 cm	NA	NA	NA	glandular, papillae	no	no	no	NA	NA	cervix	no	NA
209	SS	43/F	4201	DPV	cervical biopsy	cervix	NA	3X3X1 cm	NA	NA	NA	sheets, nests	no	no	no	NA	NA	cervix	no	NA
210	AK	50/F	1023014	AUB	hysterectomy with bso, b/l pelvic LN , para aortic LN	endometrium	polypoidal	4.5X3.5X2 cm	fundus,body	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body	no	free

				FIGO Grade	pTNM	Histological Diagnosis	IHC if available												Final Diagnosis
adnexa	LN	omentum	add features				ER	PR	Napsin A	WT1	p53	p16	Ki-67	vimentin	SMA	desmin	CD10	others	
NA	NA	NA	NA	NA	NA	ENDOCERVICAL ADENOCARCINOMA, USUAL TYPE	neg	NA	neg	neg	neg	pos	90%	focal pos	NA	NA	NA	CK7-pos, CK20-neg, PAX8-neg	ENDOCERVICAL ADENOCARCINOMA, USUAL TYPE
NA	NA	NA	NA	NA	NA	NON KERATINISING SCC	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NON KERATINISING SCC
free	free	NA	NA	NA	T1b2N1Mx	NON KERATINISING SCC	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NON KERATINISING SCC
free	NA	NA	NA	NA	T1a2NxMx	NON KERATINISING SCC	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NON KERATINISING SCC
NA	NA	NA	NA	NA	NA	NON KERATINISING SCC	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NON KERATINISING SCC
free	metastatic pelvic LN	free	NA	NA	T1b2N1Mx	ENDOCERVICAL ADENOCARCINOMA, USUAL TYPE	neg	NA	NA	neg	neg	pos	NA	neg	NA	NA	NA	NA	ENDOCERVICAL ADENOCARCINOMA, USUAL TYPE
free	free	NA	NA	NA	T1b1N0Mx	ADENOSQUAMOUS CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ADENOSQUAMOUS CARCINOMA
NA	NA	NA	NA	NA	NA	KERATINISING SCC	NA	NA	NA	NA	NA	pos	NA	NA	NA	NA	NA	p40- pos	KERATINISING SCC
free	NA	NA	NA	NA	T1a1N0Mx	NON KERATINISING SCC	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NON KERATINISING SCC
free	NA	NA	NA	II	T1aNxMx	ENDOMETRIOID CARCINOMA	NA	pos	NA	neg	NA	diffuse pos	70%	pos	NA	NA	NA	beta catenin-memb pos, CEA-neg	ENDOMETRIOID CARCINOMA
free	free	NA	senile cystic atrophy	II	T1aN0Mx	ENDOMETRIOID CARCINOMA	pos	pos	NA	neg	neg	NA	NA	NA	NA	NA	NA	MMR PROFICIENT	ENDOMETRIOID CARCINOMA
free	free	free	senile cystic atrophy	II	T1bN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	NA	I	T1aN0Mx	ENDOMETRIOID CARCINOMA	pos	weak pos	NA	NA	wild type pos	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	NA	NA	senile cystic atrophy	I	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
NA	NA	NA	NA	NA	NA	NON KERATINISING SCC	NA	NA	NA	NA	NA	diffuse strong pos	NA	NA	NA	NA	NA	p40- pos	NON KERATINISING SCC
NA	NA	NA	NA	NA	NA	ENDOCERVICAL ADENOCARCINOMA, USUAL TYPE	pos	focal weak pos	NA	neg	NA	strong pos	NA	neg	NA	NA	NA	NA	ENDOCERVICAL ADENOCARCINOMA, USUAL TYPE
NA	NA	NA	NA	NA	NA	NON KERATINISING SCC	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NON KERATINISING SCC
free	free	NA	NA	I	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA

S.no	Name	Age/Sex	MRD No.	C/P	Type of specimen	Gross						Microscopy								
						location	growth pattern	size	extension	myometrial involvement	add features	pattern	differentiation	mitosis	necrosis	myometrial involvement	solid component	extension	LV/PN invasion	parametrium
211	SG	62/F	963647	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	exophytic	5X2X1.5 cm	fundus,body,isthmus	>1/2	NA	glandular,sheets,nests	no	no	no	>1/2	>5%,<50%	fundus,body,isthmus	no	free
212	SK	64/F	147939	PMB	hysterectomy with bso,omentum, b/l pelvic LN	endometrium	polypoidal	2X2X1 cm	fundus,body,isthmus	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body,isthmus	no	free
213	S	40/F	393043	HMB	hysterectomy with bs	intramural	nodular mass	4.5X3.5X2 cm	fundus,body,isthmus	>1/2	single intramural fibroid	sheets, fascicles	no	>10/10 hpf	no	>1/2	NA	fundus,body,isthmus	no	free
214	JK	47/F	828383	DPV	cervical biopsy	cervix	NA	3X1X1 cm	NA	NA	NA	sheets, nests	no	<5/10 hpf	no	NA	NA	cervix	no	NA
215	KL	58/F	324023	AUB	Endo biopsy	endometrium	NA	0.6 cm	NA	NA	NA	glandular	no	no	no	NA	<5%	NA	no	NA
216	S	44/F	333888	AUB	endo curettes	endometrium	NA	1.5x1x0.6 cm	NA	NA	NA	glandular	no	no	no	NA	<5%	NA	no	NA
217	PK	60/F	695031	PMB	hysterectomy with bso,omentum, b/l pelvic LN	endometrium	polypoidal	2.5x1.5x1 cm	fundus,body	<1/2	NA	glandular	no	no	no	<1/2	>5%,<50%	fundus,body	no	free
218	NK	57/F	472567	AUB	hysterectomy with bso, b/l pelvic LN	endometrium	polypoidal	2.5x1.5x1 cm	fundus,body,isthmus	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body,isthmus	no	free
219	CM	73/F	925811	PMB	endo curettes	endometrium	NA	3.5X2.5X1.5 cm	NA	NA	NA	glandular,sheets,nests	squamous	<5/10 hpf	no	NA	>50%	NA	no	NA
220	CKA	57/F	615324	AUB	endo curettes for review	endometrium		NA	NA	NA	NA	glandular,sheets,nests	squamous	no	no	NA	>5%,<50%	NA	no	NA
221	KD	55/F	771176	AUB	hysterectomy with bso, b/l pelvic LN	endometrium	exophytic	3X2X1 cm	fundus,body,isthmus	>1/2	NA	glandular,sheets,nests	no	no	no	>1/2	>5%,<50%	fundus,body,isthmus	no	free
222	VS	59/F	851647	AUB	hysterectomy with bs	endometrium	exophytic	3X3X1 cm	fundus,body,isthmus	>1/2	NA	glandular	no	no	no	>1/2	<5%	fundus,body,isthmus	no	free
223	SG	69/F	203188	PMB	endo curettes	endometrium	NA	2.5X1X1 cm	NA	NA	NA	glandular	no	no	no	NA	>50%	NA	no	NA
224	TD	70/F	872924	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	exophytic	3X2X1 cm	fundus,body,isthmus	>1/2	NA	glandular	no	no	no	>1/2	<5%	fundus,body,isthmus	no	free
225	HK	66/F	884032	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	exophytic	7X3X1.8 cm	fundus,body	>1/2	NA	glandular,sheets,nests	no	no	no	>1/2	>50%	fundus,body	no	free

				FIGO Grade	pTNM	Histological Diagnosis	IHC if available												Final Diagnosis
adnexa	LN	omentum	add features				ER	PR	Napsin A	WT1	p53	p16	Ki-67	vimentin	SMA	desmin	CD10	others	
free	free	NA	NA	II	T1bN0Mx	ENDOMETRIOID CARCINOMA	pos	pos	NA	neg	wild type pos	focal pos	NA	pos	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	free	NA	I	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	NA	NA	LM	NA	T1bN0Mx	LEIOMYOSARCOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	LEIOMYOSARCOMA
NA	NA	NA	NA	NA	NA	NON KERATINISING SCC	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NON KERATINISING SCC
NA	NA	NA	NA	I	NA	ENDOMETRIOID CARCINOMA	pos	NA	NA	neg	NA	NA	NA	focal pos	NA	NA	NA	CK7-pos, CK20-	ENDOMETRIOID CARCINOMA
NA	NA	NA	atypical endometrial hyperplasia	I	NA	ENDOMETRIOID CARCINOMA	pos	NA	NA	neg	NA	pos	NA	pos	NA	NA	NA	CK7 - pos, CK20- neg	ENDOMETRIOID CARCINOMA
free	free	free	senile cystic atrophy	II	T1aN0Mx	ENDOMETRIOID CARCINOMA	pos	NA	NA	neg	focal pos	pos	20%	NA	NA	NA	NA	CK7 - pos, CK20- neg,	ENDOMETRIOID CARCINOMA
free	free	NA	NA	I	T1aN0Mx	ENDOMETRIOID CARCINOMA	pos	NA	neg	neg	NA	patchy pos	NA	pos	NA	NA	NA	CK7 - pos, CK20- neg	ENDOMETRIOID CARCINOMA
NA	NA	NA	senile cystic atrophy	III	NA	ENDOMETRIOID CARCINOMA WITH SQUAMOUS DIFF	diffuse pos	diffuse pos	neg	neg	NA	pos	NA	NA	NA	NA	NA	CK7-pos, CK20-neg, p63-neg	ENDOMETRIOID CARCINOMA WITH SQUAMOUS DIFF
NA	NA	NA	NA	II	NA	ENDOMETRIOID CARCINOMA WITH SQUAMOUS DIFF	pos	NA	NA	neg	pos	pos	NA	NA	NA	NA	NA	CK5/6-pos in squamoid comp, CEA-focal pos in	ENDOMETRIOID CARCINOMA WITH SQUAMOUS DIFF
free	free	NA	NA	II	T1bN0Mx	ENDOMETRIOID CARCINOMA	focal pos	NA	neg	neg	weak pos	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	NA	NA	NA	I	T1bN0Mx	ENDOMETRIOID CARCINOMA	pos	NA	neg	neg	focal pos	pos	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
NA	NA	NA	senile cystic atrophy	III	NA	ENDOMETRIOID CARCINOMA	diffuse pos	pos	neg	neg	weak pos	diffuse pos	NA	NA	NA	NA	NA	CK5/6-focal pos	ENDOMETRIOID CARCINOMA
free	free	NA	endometrial hyperplasia without atypia	I	T1bN0Mx	ENDOMETRIOID CARCINOMA	pos	NA	NA	neg	NA	NA	NA	NA	NA	NA	NA	MMR PROFICIENT	ENDOMETRIOID CARCINOMA
free	free	NA	senile cystic atrophy	III	T1bN0Mx	ENDOMETRIOID CARCINOMA	pos	NA	neg	neg	weak pos	NA	40%	NA	NA	NA	NA	MMR PROFICIENT	ENDOMETRIOID CARCINOMA

S.no	Name	Age/Sex	MRD No.	C/P	Type of specimen	Gross						Microscopy								
						location	growth pattern	size	extension	myometrial involvement	add features	pattern	differentiation	mitosis	necrosis	myometrial involvement	solid component	extension	LV/PN invasion	parametrium
226	ND	65/F	39758	PMB	hysterectomy with bso, b/l pelvic LN, spleen	endometrium	exophytic	9X8X6 cm	fundus,body	>1/2	NA	glandular,sheets,nests	no	<5/10 hpf	no	>1/2	>50%	fundus,body	LV +	free
227	AA	59/F	932248	AUB	hysterectomy with bso, b/l pelvic LN	endometrium	polypoidal	3x2.5x1 cm	fundus,body	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body	no	free
228	AK	81/F	935349	PMB	hysterectomy with bso,omentum, b/l pelvic LN, para aortic LN	endometrium	exophytic	6x3.5x3 cm	fundus,body,isthmus	>1/2	NA	glandular, villous	no	no	no	>1/2	<5%	fundus,body,isthmus	no	free
229	NS	64/F	967821	PMB	hysterectomy with bso,omentum, b/l pelvic LN, para aortic LN	endometrium	polypoidal	2.5x1.5x1 cm	fundus,body,isthmus	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body,isthmus	no	free
230	MK	61/F	977442	PMB	hysterectomy with bso,omentum, b/l pelvic LN	endometrium	exophytic	7X3X1.8 cm	fundus,body,isthmus	>1/2	NA	glandular,sheets,nests	no	no	no	>1/2	>50%	fundus,body,isthmus	no	free
231	PS	65/F	978752	PMB	hysterectomy with bso, b/l pelvic LN	endometrium	polypoidal	3x2.5x1 cm	fundus,body	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body	no	free
232	TK	41/F	983400	HMB	hysterectomy with bso, b/l pelvic LN	endometrium	polypoidal	6X3X1 cm	fundus,body,isthmus, endocervix	<1/2	NA	glandular	no	no	no	<1/2	<5%	fundus,body,isthmus, endocervix	no	free
233	RD	48/F	995018	AUB	hysterectomy with bso, b/l pelvic LN	endometrium	polypoidal	6X3X1 cm	fundus,body,isthmus	<1/2	NA	glandular,sheets,nests	no	<5/10 hpf	no	<1/2	>5%,<50%	fundus,body,isthmus	no	free
234	SK	60/F	1021234	PMB	endo curettes	endometrium	NA	4x2x1.5 cm	NA	NA	NA	glandular,sheets,nests	no	no	yes,<50%	NA	>50%	NA	no	NA
235	K	40/F	313289	AUB	hysterectomy for review	intramural	NA	NA	NA	NA	NA	facicles	no	<5/10 hpf	yes,>50%	NA	NA	NA	no	NA
236	MK	42/F	731327	HMB	Endo biopsy	endometrium	NA	0.6 cm	NA	NA	NA	sheets, fascicles	no	<5/10 hpf	yes,<50%	NA	NA	NA	no	NA
237	BD	54/F	232436	AUB	hysterectomy with bso	endometrium	polyp	2.5x1.5x1 cm	fundus,body	NA	NA	glandular, papillae	no	no	no	NA	>50%	fundus,body	no	NA
238	JK	53/F	292763	AUB	endometrial polyp	endometrium	polyp	1x0.8x0.3cm	NA	NA	NA	glandular	no	no	no	NA	<5%	NA	no	NA
239	RK	43/F	940338	AUB	hysterectomy with bso	cervix	endophytic	2.5x1.5x1 cm	cervix	NA	NA	sheets	no	no	no	NA	NA		LV +	involved

				FIGO Grade	pTNM	Histological Diagnosis	IHC if available												Final Diagnosis
adnexa	**LN**	**omentum**	**add features**				**ER**	**PR**	**Napsin A**	**WT1**	**p53**	**p16**	**Ki-67**	**vimentin**	**SMA**	**desmin**	**CD10**	**others**	
involved	metastatic pelvic LN	NA	senile cystic atrophy	III	T3aN1Mx	ENDOMETRIOID CARCINOMA	neg	focal pos	NA	neg	NA	pos	NA	focal pos	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	NA	I	T1aN0Mx	ENDOMETRIOID CARCINOMA	pos	pos	NA	neg	weak pos	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	senile cystic atrophy	I	T1bN0Mx	ENDOMETRIOID CARCINOMA-VILLOGLANDULAR	diffuse pos	pos	NA	neg	NA	patchy pos	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA-VILLOGLANDULAR
free	free	NA	NA	I	T1aN0Mx	ENDOMETRIOID CARCINOMA-VILLOGLANDULAR	pos	focal pos	NA	neg	NA	patchy pos	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA-VILLOGLANDULAR
free	free	free	NA	III	T1bN0Mx	ENDOMETRIOID CARCINOMA	pos	pos	NA	neg	wild type pos	patchy pos	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	senile cystic atrophy	I	T1aN0Mx	ENDOMETRIOID CARCINOMA	NA	focal pos	NA	neg	NA	patchy pos	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	free	NA	NA	I	T1aN0Mx	ENDOMETRIOID CARCINOMA	pos	pos	NA	neg	neg	patchy pos	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
involved	free	NA	NA	II	T3aN0Mx	ENDOMETRIOID CARCINOMA	pos	NA	NA	neg	wild type pos	patchy pos	15%	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
NA	NA	NA	NA	III	NA	ENDOMETRIOID CARCINOMA	focal pos	focal pos	neg	neg	NA	NA	NA	focal pos	NA	NA	NA	CK- pos	ENDOMETRIOID CARCINOMA
NA	NA	NA	NA	NA	NA	LEIOMYOSARCOMA	NA	NA	NA	NA	NA	NA	12%	pos	pos	neg	NA	CD34-neg, CD117-	LEIOMYOSARCOMA
NA	NA	NA	NA	NA	NA	LEIOMYOSARCOMA	pos	NA	NA	NA	strong pos	pos	80%	pos	pos	neg	NA	CK- pos, EMA-neg, myogeni	LEIOMYOSARCOMA
free	NA	NA	NA	III	T1aNxMx	SEROUS CARCINOMA- HIGH GRADE	neg	NA	NA	NA	NA	NA	80%	NA	NA	NA	NA	NA	SEROUS CARCINOMA-HIGH GRADE
NA	NA	NA	atypical endometrial hyperplasia	I	NA	ENDOMETRIOID CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ENDOMETRIOID CARCINOMA
free	NA	NA	NA	NA	T1b2N0Mx	SMALL CELL NEUROENDOCRINE CARCINOMA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	CK-dot like positive, chromogranin A-	SMALL CELL NEUROENDOCRINE CARCINOMA

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The Principal,
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Subject: **Approval of Plan of Thesis.**

This is to inform you that the Faculty of Medical Sciences in its meeting held on 22.01.2021 has approved the plan of thesis of **Dr. Sargun Grewal,** a student of your college for **MD Pathology** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis
Histomorphological spectrum of malignant uterine neoplasms

Supervisor
Dr. Aminder Singh
Assoc. Prof.,
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Co-Supervisor
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Prof.,
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The student has to submit the three copies of thesis (along with PDF format) , to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She must directed to attach a photocopy of this letter with the forwarding letter while submitting thesis to the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic,(if any).

Dr. S P Singh MS(Oph)
Controller of Examinations

Note :

1. ***If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.***
2. *The student may submit the thesis as per the schedule already conveyed i.e for May/June examination 30th Nov of the preceding the year of examination and for Nov/Dec examinations 31st May of the year of examination.*

HISTOMORPHOLOGICAL SPECTRUM OF MALIGNANT UTERINE NEOPLASMS

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED

IN PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

MD

In

PATHOLOGY

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES

FARIDKOT

NOVEMBER, 2019

DR. SARGUN GREWAL

DEPARTMENT OF PATHOLOGY
DAYANAND MEDICAL COLLEGE AND HOSPITAL
LUDHIANA

ABSTRACT OF PLAN OF THESIS

Title	HISTOMORPHOLOGICAL SPECTRUM OF MALIGNANT UTERINE NEOPLASMS
For the degree of	MD (PATHOLOGY)
Name of the candidate	Dr. Sargun Grewal
Supervisor	Dr Aminder Singh, Associate Professor, Department of Pathology, DMCH, Ludhiana
Co-supervisor	Dr Neena Sood, Professor & Head, Department of Pathology, DMCH, Ludhiana. Dr. Harpreet Kaur, Professor, Department of Pathology, DMCH, Ludhiana.
Institution	Dayanand Medical College and Hospital, Ludhiana
University	Baba Farid University of Health Sciences, Faridkot

Introduction: This 5 year study, of which 3.5 years (June 2016-December 2019) is retrospective and 1.5 years (January 2020-June 2021) is prospective, will be conducted in the Department of Pathology, Dayanand Medical College and Hospital, Ludhiana. All the cases suspected of malignant uterine neoplasms will be analyzed and correlated with Immunohistochemistery (IHC) studies.

Aims & Objectives: To study the detailed histomorphological features of malignant uterine neoplasms and correlate these features with immunohistochemical (IHC) findings.

Material & Methods: This study will be conducted in the Department of Pathology at Dayanand Medical College and Hospital, Ludhiana for a period of 5 years, of which 3.5 years (June 2016- December 2019) will be retrospective and 1.5 years (January 2020-June 2021) will be prospective. All specimens of malignant tumors of uterus and cervix received in the histopathology lab of the department will be processed and its morphology will be analysed under the light microscope. Immunohistochemical staining will be done in the immunopathology laboratory.

Clinical Significance: To obtain a good database for assessment and diagnosis of malignant uterine neoplasms based on the histomorphological and IHC findings.

Keywords: malignant, uterus, cervix, epithelial, mesenchymal, immunohistochemistery (IHC)

(Signature)	(Signature)	(Signature)	(Signature)	(Signature)
Candidate	Co-supervisor	Co-supervisor	Supervisor	Principal

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled **"HISTOMORPHOLOGICAL SPECTRUM OF MALIGNANT UTERINE NEOPLASMS"** exist in the Department of Pathology, DMC&H, Ludhiana and will be provided to the candidate. We will see that the data being included in the thesis is genuine and is collected by the candidate herself under our supervision and guidance.

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Place : Ludhiana

Date : December 2019

APPROVAL PROFORMA
BY
RESEARCH & ETHICAL COMMITTEE
DAYANAND MEDICAL COLLEGE & HOSPITAL, LUDHIANA

Name of candidate	Dr. Sargun Grewal
Department	Pathology
Topic of Thesis	HISTOMORPHOLOGICAL SPECTRUM OF MALIGNANT NEOPLASMS
Likely date of appearing in PG examination	May 2022
Date of enrollment	18th May, 2019
Name of Head of Department	Dr. Neena Sood
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Dr. Jaspal Singh (Professor & Head, Surgery)	Mr. A K Jindal (Member, Ethics Committee)
Dr. Dinesh Gupta (Professor & Head, Medicine)	Dr. Anu Sharma (Professor, Anatomy)
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Approved: Yes / ~~No~~

Dr. Sandeep Puri
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Research Committee

Chairperson
Research Committee

Approved: Yes / ~~No~~

Prof. Arvind Malhotra
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Ethics Committee

BABA FARID UNIVERSITY OF HEALTH SCIENCES, FARIDKOT

PROFORMA FOR REGISTRATION OF SUBJECT FOR DISSERTATION

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2	NAME OF THE INSTITUTE	Dayanand Medical College and Hospital, Ludhiana
3	COURSE OF STUDY AND SUBJECT	MD Pathology
4	DATE OF ADMISSION OF COURSE	18-05-2019
5	TITLE OF THE TOPIC	HISTOMORPHOLOGICAL SPECTRUM OF MALIGNANT UTERINE NEOPLASMS

6. BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

Uterine tumors are a heterogeneous group of neoplasms and are diagnostically challenging. They are broadly divided into cervical, endometrial, mesenchymal and mixed epithelial and mesenchymal tumors. Due to lack of cancer awareness and variable pathology they have become an important public health issue. According to a study done by Ramnath Takiar et al, gynecological cancers have increased in India and are estimated to be around 182,602 by the year 2020 constituting about 30% of the total cancers among women in India, cancer of the uterine cervix followed by ovary and corpus uteri being the major contributors.[1]

Cervical cancer is the fourth most common cancer among women globally and the second most common cancer among Indian women. India alone bears 23% of the global cervical cancer burden. Precancerous changes are usually asymptomatic and can be assessed on cervical smear. But a cervical biopsy is crucial to determine various prognostic factors such as the tumor grade, depth and width of invasion and presence of invasion of lymphovascular space. The International Federation of Gynaecology and Obstetrics (FIGO) staging system is widely accepted and most commonly used. It takes into account the physical examination, colposcopy findings, histopathology and radiology.[2]

Endometrial carcinoma is the most common invasive cancer of the female genital tract and accounts for 7% of all the invasive cancers in women.[3] According to a consensus document by the Indian Council of Medical Research, the total number of estimated new cases of endometrial cancer in 2018 in India were 13,328 with an estimated 5010 deaths. Clinically women can present with various symptoms such as vaginal bleeding, pelvic pain, spotting, leucorrhoea and rarely with an asymptomatic course. Endometrial biopsy is the gold standard method for distinguishing normal endometrium from pathological endometrium.[4]

Soft tissue sarcomas of the uterus are a varied group of neoplasms, all of mesenchymal origin. They are rare but aggressive, comprising 3–7% of all uterine malignancies. It is difficult to distinguish between uterine sarcomas and other uterine tumors clinically and is hence reliant on histological and imaging features. A rapidly growing fibroid/uterine mass in a peri- or postmenopausal women should raise a suspicion and a biopsy should be considered to determine the pathology. Amongst these, leiomyosarcomas are the commonest in India as proved by a retrospective study conducted over a period of 8 years by Nusrath et al, in which total of 11 cases of uterine sarcoma were diagnosed. Out of these, 6 patients had leiomyosarcoma (54.5%), 4 had endometrial stromal sarcoma (36%), and only 1 had adenosarcoma (9%).[5]

Immunohistochemical (IHC) studies have steadily advanced and developed thus becoming one of the main diagnostic tools in anatomic pathology in general. It can be employed to investigate the earliest changes in transformed tissues, identifying cellular changes not normally visible with hematoxylin and eosin (H&E) stain.[6] Regardless of the primary diagnosis, no therapeutic intervention should be initiated without correlation with IHC markers wherever possible. Markers of cell proliferation such as Ki-67 along with p53 protein, estrogen receptor (ER), progesterone receptor (PR), PAX-8, WT-1 and Napsin A, are successfully being used to differentiate between benign and malignant tumors.[7,8]

This present study is intended to ascertain a correlation between the histomorphological features and IHC findings wherever possible in suspected cases of malignant tumors of the uterus to aid in their definitive diagnosis.

6.2 REVIEW OF LITERATURE

The World health organization (WHO) 2014 classifies malignant uterine tumors as follows:

TUMORS OF UTERINE CERVIX

Broadly they cover epithelial, glandular, mesenchymal and mixed mesenchymal and epithelial tumors.

Epithelial: Squamous cell carcinoma-Keratinizing, Non-keratinizing, Papillary, Basaloid, Warty, Verrucous, Lymphoepitheloma-like

Glandular: Adenocarcinoma, Endocervical adenocarcinoma, Mucinous carcinoma (Gastric type, Intestinal type, Signet-ring cell type),Clear cell carcinoma, Serous carcinoma, Adenosquamous carcinoma, Adenoid basal carcinoma, Adenoid cystic carcinoma and Undifferentiated carcinoma

Mesenchymal: Leiomyosarcoma, Rhabdomyosarcoma

Mixed epithelial and mesenchymal tumours: Adenosarcoma and Carcinosarcoma

Out of these, the main type is squamous cell carcinoma (up to 9 out of 10 cases). They most often begin in the transformation zone (where the ectocervix joins the endocervix) and develop from the cells of ectocervix. On histology, the cancer cells have features of squamous cells.

Other commonly occurring amongst cervical cancers, are Adenocarcinomas. They develop from the mucus-producing gland cells of the endocervix. Rarely, cervical cancers present as adenosquamous carcinomas or mixed carcinomas, having feature of both squamous cell carcinomas and adenocarcinomas.[9]

Federation of gynecology and obstetrics (FIGO) staging of carcinoma of the cervix uteri (2018) broadly comprises of the following stages:

Stage I: The carcinoma is strictly confined to the cervix uteri (extension to the corpus should be disregarded), **Stage II**: The carcinoma invades beyond the uterus, but has not extended, **Stage III**: The carcinoma involves the lower third of the vagina and/or extends to the pelvic wall

and/or causes hydronephrosis or non-functioning kidney, **Stage IVA-** Spread of the growth to adjacent organs, **IVB-** Spread to distant organs Involvement of vascular/lymphatic spaces does not change the staging. The lateral extent of the lesion is no longer considered.[10]

TUMORS OF THE UTERINE CORPUS

EPITHELIAL TUMORS:

Endometrial carcinoma:

- Endometrioid adenocarcinoma, usual type
- Endometrioid adenocarcinoma, variant types- squamous differentiation, villoglandular, secretory, ciliated cell
- Mucinous carcinoma
- Serous carcinoma
- Clear cell carcinoma
- Mixed cell adenocarcinoma
- Undifferentiated carcinoma

Out of these endometrioid carcinoma is the commonest and accounts for 85% of the newly diagnosed cases, serous carcinoma represents 3-10% and clear cell carcinoma accounts for <5% of the diagnosed cases.

Endometrioid carcinomas grossly can present in the form of localized polypoid tumor or diffusely infiltrating the endometrial lining. On histology they are mainly composed of glands exhibiting complex architecture, extensive branching and papillary patterns not found in a normally proliferating endometrium. Architectural grading defined by the International Federation of Gynecology and Obstetrics (FIGO), divides endometrioid carcinoma into grade 1 (well differentiated)- exclusively composed of glands without intervening stroma (less than or equal to 5% solid growth) , grade 2 (moderately differentiated)- glands mixed with 6-50% solid growth and grade 3 (poorly differentiated)- >50% solid growth.

Serous carcinoma grossly presents as a large bulky tumor or invading deeply into the myometrium. On histology they display glandular and

papillary growth with marked cytological atypia and atypical mitotic figures.

Clear cell carcinoma is composed of cells with high grade nuclei and clear cytoplasm arranged in either tubulocystic, papillary or solid pattern.[11]

A study by Yemelyanova A et al illustrated 90-100% p16 expression in cells of serous carcinoma compared to 10-90% cells of grade 3 endometrioid carcinoma.[12] Another study by Gilks CB, concluded that serous carcinoma are positive for PTEN, diffusely positive for p16, aberrant mutation type expression with p53 and negative for both ER and PR. Grade 3 endometrioid carcinoma on the other hand was positive for ER and PR, focally positive for p16, wild type staining for p53 and negative for PTEN.[13] In a study by Gian Franco in June 2019, out of 45 endometrial clear cell carcinoma, fifteen patients showed loss of one or more mismatch repair proteins. All cases were negative for ER and PR, a "patchy" positive for p16 and exhibited a "wild type" staining pattern for p53. 40/45 (88.8%) cases showed positive staining for Napsin A.[14]

FIGO staging system for endometrial carcinomas, based on site and extent of tumor, divides it into stages I-IV. Stage I-tumor confined to the uterus. Stage II- tumor invades the stromal connective tissue of the cervix but does not extend beyond the uterus. Stage III- tumor extends beyond the uterus without distant metastasis (i.e-not outside true pelvis) Stage IV- bladder/bowel mucosa or distant spread.[15]

MESENCHYMAL TUMORS:

Uterine Leiomyosarcoma (ULMS) – mainly two variants noted, epithelioid variant and myxoid variant.

ULMS are the most commonly occurring malignant uterine neoplasms. They make up 25% of the total mesenchymal uterine tumors.

Grossly a large (usually >10cm) firm, poorly circumscribed solitary mass within the uterine cavity is identified.[16] Histomorphologicaly they are hypercellular tumors characterized by increased mitotic activity (more than or equal to 5 mitosis/10 high power field), diffuse nuclear atypia and coagulative tumor cell necrosis.[17]

FIGO staging for ULMS as collected from international journal of gynecology and obstetrics,2009: stage I- tumor limited to the uterus(Ia-<5cm ,Ib->5cm), stage II- tumor extends beyond the uterus but within the pelvis(IIa-adnexal involvement IIb-involvement of other pelvic tissues), stage III- tumor invades the abdominal tissue(IIIa- one site, IIIb- more than one site,IIIc-metastasis to pelvic and/or para-aortic lymph nodes), stage IVa- tumor invades bladder and /or rectum and IVb- distant metastasis.

On IHC they show co-expression of SMA, desmin and h-caldesman. Other than these Ki-67, p53 and ER and PR steroid receptors are amongst the chief markers.[18]

K. Mayerhofer et al. (2004), demonstrated higher Ki-67 expression in ULMS vs STUMP (smooth muscle tumor of undetermined potential) and ULMS vs LM (leiomyoma). Mittal and Demopoulos (2001) gave similar results depicting higher ki-67 expression in ULMS. In 2009, Lee et al, reported that ki-67 both independently and is association with markers like p16 and p53, demonstrated 92% sensitivity and 98% specificity for ULMS.[19,20,21]

Bcl-2 expression helps to determine the survival rates in ULMS cases. In 2016, a study done by Graaff et al. reported that Bcl-2 protein expression might contribute to a higher chemoresistance in ULMS. Observations made by D'Angelo et al. (2011) revealed that the tumors that were ki-67 positive and Bcl-2 negative had the worst prognosis.[22,23]

MIXED EPITHELIAL AND MESENCHYMAL TUMORS:

- Adenosarcoma
- Carcinosarcoma/mixed Mullerian tumors
- Endometrial stromal sarcoma

Adenosarcomas are composed of benign epithelial component and low grade malignant sarcomatous component. They grow within the endometrial cavity as a solitary polypoidal mass arising usually from the uterine fundus. Histomorphologically they are hypercellular with

typically more than or equal to 2 mitosis/ 10HPF.[23] On IHC, areas with sarcomatous overgrowth show ER, PR, WT1 and CD 10 positivity.[18]

Carcinosarcomas (malignant mixed Mullerian tumors) are bulky and necrotic polypoidal tumors filling the endometrial cavity. They have a biphasic morphology with an admixture of malignant epithelial and mesenchymal elements. The epithelial component is glandular and may have an endometrioid, serous, mucinous or clear cell differentiation. The sarcomatous component can be homologous represented by leiomyosarcoma, undifferentiated sarcoma, fibrosarcoma or endometrial stromal sarcoma or heterologous represented by either chondroid, osteoid, melanocytic, angiomatoid or rhabdomyoblastic element. On IHC the epithelial component shows diffuse positivity for pan-cytokeratins. Both epithelial and mesenchymal components together show positivity for p53.[24]

Endometrial stromal sarcoma (ESS) are neoplasms of relatively younger premenopausal women. In 2014, Conklin et al presented the new WHO classification of ESS dividing it into 4 main categories: endometrial stromal nodule, low grade ESS, high grade ESS and undetermined uterine sarcoma.[25] Histomorphologicaly they are characterized by an infiltrative tongue -like pattern often accompanied with lymphovascular space invasion. The cells are spindled to ovoid and have a hyperchromatic nucleus with regular contours and an inconspicuous nucleoli.[24] IHC helps in differentiating between low and high grade ESS. Both high grade and at times low grade tumors show positivity for cyclind1 but low grade tumors also show diffuse positivity for ER and PR receptors, CD10 and WT1.

FIGO staging for uterine ESS and Adenosarcoma compiled from the international journal of gynecology and obstetrics, 2009: stage I- tumor limited to the uterus(Ia-tumor limited to the endometrium/endocervix with no myometrial invasion, Ib- less than half or half myometrial invasion, Ic- more than half myometrial invasion), stage II- tumor extends beyond the uterus but within the pelvis (IIa- adnexal involvement IIb-involvement of other pelvic tissues), stage III- tumor invades the abdominal tissue (IIIa- one site, IIIb- more than one

site, IIIc-metastasis to pelvic and/or para-aortic lymph nodes), stage IVa- tumor invades bladder and /or rectum and IVb- distant metastasis.[18]

6.3 AIMS AND OBJECTIVES OF THE STUDY

To study the detailed histomorphological features of malignant uterine neoplasms and correlate these features with immunohistochemical (IHC) findings.

7. MATERIALS AND METHODS

7.1 Source of Data

All the malignant hysterectomy specimens, malignant cervical, endometrial/myometrial biopsies/curettings received in the Department of Pathology of Dayanand Medical College and Hospital, Ludhiana over a period of one and half years prospective and three and a half years retrospectively (total 5 years study) will be analysed.

7.2 METHOD OF COLLECTION OF DATA

INCLUSION CRITERIA

1. All malignant cervical and uterine specimens
2. Prepared and stained slides for review for uterine and cervical malignancies from an outside center.

EXCLUSION CRITERIA-

All non- malignant neoplasms of uterus and cervix.

PROCEDURE

Tissue from the cervix and uterus will be received from gynecology and Oncology department. For prospective study tissue will be processed and H&E staining will be analysed under light microscope. Diagnosis will be made based on histological features and correlated with IHC markers for confirmation of diagnosis wherever possible. For retrospective cases, the slides will be reexamined and evaluated as per proforma.

DURATION OF STUDY

Five year study of which one and half year (January 2020-June 2021) will be prospective study and three and a half years (June 2016-December 2019) will be retrospective study.

OUTCOME

All the findings will be documented according to the protocol and categorized according to the WHO classification for malignant uterine neoplasms. The histopathological findings will be correlated with the IHC findings.

STATISTICAL ANALYSIS

All data obtained will be analysed and expressed in the form of descriptive statistics.

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

Not Applicable

7.4 HAS ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

Yes

8. LIST OF REFERENCES

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PROFORMA

Sr. No. _____

Name Age Sex

MRD No. Date

Histopath No. Address

Brief history:

Investigations (Any radiological/ biochemical findings):

Type of specimen:

Gross examination:

Microscopic examination:

IHC (if done):

Final histopathological diagnosis:

Signature of Candidate **Signature of Co-Supervisor** **Signature of Supervisor**